

Clinical Trial Protocol

Iranian Registry of Clinical Trials

29 May 2026

The effect of intramuscular naloxone in comparison with intravenous naloxone inpatients with methadone overdose, a randomized clinical trial study

Protocol summary

Study aim

Determination of effects, complications, benefits, and feasibility of intramuscular naloxone

Design

Randomised (with the parallel control group), superiority, single-blinded trial. Randomisation will carry out at two different centers. The intervention group is Intramuscular naloxone and the control group is naloxone infusion which will be selected based on convenience sampling. The sample size is calculated based on a pilot study on 15 patients in each group, showing apnea/re-narcosis in 20% calculating with a power of 80%. $\alpha=5\%$, 199 cases in each group.

Settings and conduct

All the patients in the two centers of Tehran and Gorgan will be recruited to take Intramuscular or intravenous naloxone. Except for the study analyzer, all other people are not blinded to the study due to injection issues (one-sided blinded). Both groups will take intravenous naloxone and for maintenance treatment, they will get either 2/3 of the initial bolus dose i.v. hourly or they will get intramuscular injections every 4 hours in the following groups: 0.4, 0.8, 1.2, or 1.6 mg.

Participants/Inclusion and exclusion criteria

Inclusion criteria: methadone overdose as the main drug, age over 18 and under 60, no background diseases, complete response to naloxone, opioid dependant

Intervention groups

Intramuscular injection of naloxone in the case group and intravascular infusion of naloxone in the case group. The variables of the study will be evaluated through the differences between the two routes of naloxone injection interventions.

Main outcome variables

Re-narcosis; Withdrawal Syndrome; Intubation; Hospital Stay

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20120629010133N6**

Registration date: **2023-01-01, 1401/10/11**

Registration timing: **prospective**

Last update: **2023-01-01, 1401/10/11**

Update count: **0**

Registration date

2023-01-01, 1401/10/11

Registrant information

Name

Hossein Hassanian-Moghaddam

Name of organization / entity

Shahid Beheshti University of Medical Sciences

Country

Iran (Islamic Republic of)

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+98 21 5542 4041

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hassanian@sbmu.ac.ir

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-01-20, 1401/10/30

Expected recruitment end date

2024-01-20, 1402/10/30

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

The effect of intramuscular naloxone in comparison with intravenous naloxone inpatients with methadone overdose, a randomized clinical trial study

Public title

Intramuscular Naloxone in methadone overdose

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

methadone overdose as the main substance age \geq 18
age \leq 60 no background diseases response to naloxone
in initial try opioid dependent

Exclusion criteria:

no informed consent

Age

From **18 years** old to **60 years** old

Gender

Both

Phase

3

Groups that have been masked

- Data analyser

Sample size

Target sample size: **398**

Randomization (investigator's opinion)

Not randomized

Randomization description

Blinding (investigator's opinion)

Single blinded

Blinding description

Only data analyzer is not aware of the groups. Patients, assessors, physicians, and nurses are aware of the route of administration (IM vs. IV)

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Shahid Beheshti University of
Medical Sciences

Street address

5th floor, bulding no 2, Shahid Aarabi St, Yaman St.

City

Tehran

Province

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Postal code

1985717443

Approval date

2022-12-04, 1401/09/13

Ethics committee reference number

IR.SBMU.RETECH.REC.1401.580

Health conditions studied

1

Description of health condition studied

methadone

ICD-10 code

T40.3

ICD-10 code description

Poisoning by, adverse effect of and underdosing of
methadone

Primary outcomes

1

Description

Renarcosis

Timepoint

On-arrival blood gas analysis and then each 4 hours

Method of measurement

Blood gas

2

Description

Withdrawal syndrome

Timepoint

On-arrival band then each 4 hours

Method of measurement

Evaluation of COWS scale

3

Description

Need for naloxone

Timepoint

Each hour

Method of measurement

Blood gasometry, reduced respiratory rate, Apnea

4

Description

Need for intubation

Timepoint

hourly

Method of measurement

Clinical and laboratory indications for intubation

Secondary outcomes

1

Description

Hospitalization period
Timepoint
End of hospitalization
Method of measurement
Days of hospitalization

Intervention groups

1

Description

Intervention group: Intramuscular injection of naloxone would be calculated every 4 hours based on the calculation for I.V. naloxone: If the calculated dose is less than 0.2 mg/h, then naloxone IM would be 0.4 mg every 4 hours. if the calculated amount is between 0.2-<0.4, then naloxone IM would be 0.8 mg every 4 hours. if the calculated dose is between 0.4-<0.6, then naloxone IM would be 1.2 mg every 4 hours. For amounts above 0.6 mg, the IM dose would be 1.6 mg every 4 hours.

Category

Treatment - Drugs

2

Description

Control group: The routine treatment of methadone poisoning including I.V. naloxone infusion, in which it would be 2/3 of the response dose in the emergency department every hour.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Loghaman Hakim Hospital

Full name of responsible person

Ali Jangjou

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Kamali Ave, South Karegar

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2

Recruitment center

Name of recruitment center

Imam Hossein Hospital

Full name of responsible person

Farangis Sadeghi

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

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Full name of responsible person

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Grant name

Grant code / Reference number

32908

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

Yes

Title of funding source

Shahid Beheshti 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

Shahid Beheshti University of Medical Sciences

Full name of responsible person

Hossein Hassanian-Moghaddam

Position

Associate Professor

Latest degree

Subspecialist

Other areas of specialty/work

Toxicology

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Person responsible for updating data

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Position

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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