

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

10 Jun 2026

### **Analgesic effect of combining Midazolam, Morphine and Diphenhydramine for acute postoperative pain management, A comparative study**

#### **Protocol summary**

##### **Study aim**

Evaluation of the analgesic effect of morphine-ketamine-midazolam combination after surgery

##### **Design**

Clinical trial with control group, with parallel groups, double-blind, randomized, phase 2 on 66 patients. The rand function of the Excel software was used for randomization.

##### **Settings and conduct**

This study is a clinical trial performed at Sina Hospital, Tehran University of Medical Sciences. Patients are extubated after surgery and recover. In recovery, patients were evaluated based on VAS or Richmond criteria, and if they had a VAS > 4 score or Richmond +2 and above, they entered the study and were randomly assigned to one of the two groups. The first group received 2 cc of the first three drug combinations (including 20 mg of morphine -50 mg of ketamine-5 mg of midazolam, the volume of which was increased to 10 cc with distilled water). The second group received a combination of the second three drugs (including 20 mg of morphine -50 mg of ketamine -50 mg of diphenhydramine, the volume of which is 10 cc with distilled water). Then, the time of starting the effect of the drug, change of VAS or RICHMOND Agitation Sedation scale, stability of the drug effect in patients, nausea and vomiting, blood pressure and heart rate of patients and in the first time of drug application and drug use are recorded in the first 24 hours.

##### **Participants/Inclusion and exclusion criteria**

Inclusion criteria:1- Age 20 to 65 years. 2- Restorative surgery 3- Need for postoperative analgesia Exclusion criteria: 1-Drug addiction 2- History of heart disease, kidney, liver and glaucoma.3-History of psychotropic drugs and anti-nausea and vomiting

##### **Intervention groups**

All elective patients undergo reconstructive surgery

##### **Main outcome variables**

The severity of the pain heart beat blood pressure

Anxiety

#### **General information**

##### **Reason for update**

##### **Acronym**

##### **IRCT registration information**

IRCT registration number: **IRCT20130304012695N2**

Registration date: **2020-05-26, 1399/03/06**

Registration timing: **retrospective**

Last update: **2020-05-26, 1399/03/06**

Update count: **0**

##### **Registration date**

2020-05-26, 1399/03/06

##### **Registrant information**

##### **Name**

mohammadreza khajavi

##### **Name of organization / entity**

##### **Country**

Iran (Islamic Republic of)

##### **Phone**

+98 21 6312 1220

##### **Email address**

khajavim@tums.ac.ir

##### **Recruitment status**

**Recruitment complete**

##### **Funding source**

##### **Expected recruitment start date**

2019-01-21, 1397/11/01

##### **Expected recruitment end date**

2019-12-22, 1398/10/01

##### **Actual recruitment start date**

2019-02-20, 1397/12/01

##### **Actual recruitment end date**

2019-11-22, 1398/09/01

##### **Trial completion date**

2019-12-22, 1398/10/01

### Scientific title

Analgesic effect of combining Midazolam, Morphine and Diphenhydramine for acute postoperative pain management, A comparative study

### Public title

Analgesic effect of combining Midazolam, Morphine and Diphenhydramine for acute postoperative pain management, A comparative study

### Purpose

Treatment

### Inclusion/Exclusion criteria

#### Inclusion criteria:

Patients are extubated after surgery and recover. In recovery, patients were evaluated based on VAS or Richmond criteria, and if they had a VAS > 4 score or Richmond +2 and above, they entered the study and were randomly assigned to one of the two groups.

#### Exclusion criteria:

opioids addiction, underlying ischemic cardiac diseases, renal function and liver function diseases, history of allergic reaction to any of the medications used, and use of any antiemetic and antipsychotic medications, PONV and glaucoma.

### Age

From **20 years** old to **65 years** old

### Gender

Both

### Phase

3

### Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

### Sample size

Target sample size: **66**

Actual sample size reached: **66**

### Randomization (investigator's opinion)

Randomized

### Randomization description

The sampling is done by easy burst method and according to patient referral to recovery room. Randomization method is balanced block randomization and will be done by Randlist software.

### Blinding (investigator's opinion)

Double blinded

### Blinding description

The person who makes the medicine add a code to every single medicine. The person who injects the drug does not know the code. The patient is not aware of the type of injectable medication. The researcher is not aware of the type of drug during the study.

### Placebo

Not used

### Assignment

Parallel

### Other design features

## Secondary Ids

empty

## Ethics committees

### 1

#### Ethics committee

##### Name of ethics committee

Ethics committee of .tehran University of Medical Sciences

##### Street address

sina hospital, imam khomeini st.

##### City

tehran

##### Province

Tehran

##### Postal code

1136746911

#### Approval date

2018-11-19, 1397/08/28

#### Ethics committee reference number

IR.TUMS.IKHC.REC.1397.224

## Health conditions studied

### 1

#### Description of health condition studied

postoperative pain

#### ICD-10 code

S66.0

#### ICD-10 code description

Injury of long flexor muscle, fascia and tendon of thumb at wrist and hand level

## Primary outcomes

### 1

#### Description

The effect of the drug combination of midazolam, diphenhydramine and morphine on pain relief

#### Timepoint

In 5, 10, 15, 30 minutes after the operation, the severity pain was measured

#### Method of measurement

visual analog scal

## Secondary outcomes

### 1

#### Description

patients' agitation evaluation

#### Timepoint

In 5, 10, 15 and 30 minutes after surgery

#### Method of measurement

richmond agitation scale

## Intervention groups

### 1

#### Description

Intervention group: Morphine, Midazolam, In this group, in a syringe of 10 cc, 10 mg of morphine, 100 mg of diphenhydramine and 10 mg of midazolam, prepared then increase the volume to 10 cc with distilled water. In patients who have pain and want to take analgesia, we inject one cc of this medicine mixture. Two minutes after the injection, if the pain is not controlled, we take another cc of this mixture. we record the number of injections and reduce the severity of the pain and the duration of the pain reduction per minute.

#### Category

Treatment - Drugs

### 2

#### Description

Control group: Morphine, ketamine, Diphenhydramine. In this group, in a syringe of 10 cc, 10 mg of morphine, 100 mg of diphenhydramine and 10 mg of ketamine, prepared then increase the volume to 10 cc with distilled water. In patients who have pain and want to take analgesia, we inject one cc of this medicine mixture. Two minutes after the injection, if the pain is not controlled, we take another cc of this mixture. we record the number of injections and reduce the severity of the pain and the duration of the pain reduction per minute.

#### Category

Treatment - Drugs

## Recruitment centers

### 1

#### Recruitment center

##### Name of recruitment center

sina hospital

##### Full name of responsible person

mohammadreza khajavi

##### Street address

sina hospital, imam khomeini st.

##### City

tehran

##### Province

Tehran

##### Postal code

1136746911

##### Phone

+98 21 6634 8500

##### Email

khajavim@tums.ac.ir

## Sponsors / Funding sources

### 1

#### Sponsor

Name of organization / entity

Tehran University of Medical Sciences

#### Full name of responsible person

mohammad ali sahraeian

#### Street address

Keshavarz Blvd., corner of Quds St., Central Organization of Tehran University of Medical Sciences

#### City

tehran

#### Province

Tehran

#### Postal code

1417653761

#### Phone

+98 21 8163 3685

#### Email

vcr@tums.ac.ir

#### Grant name

#### Grant code / Reference number

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

Yes

#### Title of funding source

Tehran 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

Tehran University of Medical Sciences

##### Full name of responsible person

Mohammadreza Khajavi

##### Position

Professor

##### Latest degree

Specialist

##### Other areas of specialty/work

Anesthesiology

##### Street address

Central building of Tehran University of Medical sciences, Ghods st., Keshavarz blv.

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## Person responsible for scientific inquiries

### Contact

**Name of organization / entity**

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**Full name of responsible person**

Mohammadreza Khajavi

**Position**

Professor

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## Person responsible for updating data

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**Name of organization / entity**

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Mohammadreza Khajavi

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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**

No - There is not a plan to make this available

**Data Dictionary**

Undecided - It is not yet known if there will be a plan to make this available