Clinical Trial Protocol
Iranian Registry of Clinical Trials

29 Jul 2026

Comparing the effect of intravenous midazolam and oral melatonin on controlling agitation caused by ketamine in emergency department

Protocol summary

Study aim
Comparing the effect of intravenous midazolam and oral melatonin on controlling agitation caused by ketamine in emergency department

Design
Prospective clinical trial with parallel control group, double-blind, randomized with the table of random numbers

Settings and conduct
In this study, 96 patients who are candidate for receiving Ketamine in emergency department of Al-Zahra and Kashani hospitals in Isfahan are divided into three groups using randomized blocking method. The drugs are prepared and packaged by the pharmacology department. The first group is treating with intravenous midazolam and oral placebo and the second group is treated with oral melatonin and intravenous placebo. The third group is control group that is treated with oral and intravenous placebo. Thirty minutes after receiving this intervention, patients are receiving 1-2 mg/kg intravenous Ketamine during 30-60 seconds and then receiving 0.25-0.5 mg/kg intravenous Ketamine every 10 minutes as a maintenance dose (maximum 5 mg/kg).

Participants/Inclusion and exclusion criteria
Inclusion criteria: All patients who aged more than 18 years who are the candidate for receiving Ketamine as an anesthesia for small surgeries. Exclusion criteria: Patients with fever, obesity, head trauma, hydrocephaly, glaucoma, and psychological disorders.

Intervention groups
In this study all patients are receiving intravenous Ketamine as an anesthesia. Patients in the first group are receiving intravenous Midazolam and oral placebo, 30 minutes before receiving Ketamine. Patients in the second group are receiving oral Melatonin and intravenous placebo, 30 minutes before receiving Ketamine. Patients in the third group are receiving oral and intravenous olacebo, 30 minutes before receiving Ketamine.

Main outcome variables
Richmond Agitation Scale

General information

Reason for update
Acronym
IRCT registration information
IRCT registration number: **IRCT20180129038549N8**
Registration date: **2018-09-24, 1397/07/02**
Registration timing: **retrospective**

Last update: **2018-09-24, 1397/07/02**
Update count: **0**
Registration date
2018-09-24, 1397/07/02

Registrant information
Name
Farhad Heydari
Name of organization / entity
Country
Iran (Islamic Republic of)
Phone
+98 31 3786 8804
Email address
drfarhadheydari@gmail.com

Recruitment status
Recruitment complete
Funding source

Expected recruitment start date
2017-06-22, 1396/04/01
Expected recruitment end date
2018-03-21, 1397/01/01
Actual recruitment start date
2017-03-21, 1396/01/01
Actual recruitment end date
2018-03-21, 1397/01/01

Trial completion date
2018-03-21, 1397/01/01

Scientific title
Comparing the effect of intravenous midazolam and oral melatonin on controlling agitation caused by ketamine in emergency department

Public title
Reduction of agitation associated with ketamine

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Age over 18 years old Receiving ketamine as an anesthetic agent for small surgeries Patient's consent to participate in the study

Exclusion criteria:
Fever Obesity (BMI>30) Head trauma with loss of consciousness Brain tumor, Hydrocephaly Glaucoma Psychosis Psychological disorders History of using Benzodiazepine during last two weeks

Age
From **18 years** old

Gender
Both

Phase
3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

Sample size
Target sample size: **96**
Actual sample size reached: **96**

Randomization (investigator's opinion)
Randomized

Randomization description
After the arrival of the patients to the emergency department, they are divided into 3 groups by a computer-generated random number table with 4 blocks.

Blinding (investigator's opinion)
Double blinded

Blinding description
To make sure of the double-blind protocol of the study, preparation of the solutions, injections, and registration of the results were carried out by the pharmacology department. The packets were named A, B, and C following the codes. In one packet, there are intravenous midazolam and oral placebo, in the second packet, there is an equal volume of intravenous placebo and the oral melatonin, and in another packet, there is intravenous and oral placebo. Patients are randomized to receive one of the packets. The patients and their parents and the nurses are unaware of the contents of the drugs. Data collectors, outcome assessors, and data analysts are all kept blinded to the allocation.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics committee of Isfahan University of Medical Science

Street address
Isfahan University of Medical Science, Hezarjrib Street, Isfahan City

City
Isfahan

Province
Isfehan

Postal code
8174673461

Approval date
2017-06-20, 1396/03/30

Ethics committee reference number
IR.MUI.REC.1396.30.33

Health conditions studied

1

Description of health condition studied
Agitation

ICD-10 code
R45.1

ICD-10 code description
Restlessness and agitation

Primary outcomes

1

Description
Richmond Agitation Scale score

Timepoint
Every 5 minutes after ketamine administration

Method of measurement
Richmond Agitation Scale table

Secondary outcomes

empty

Intervention groups

1

Description
Intervention group 1: In this group patients are receiving 0.05 mg/kg intravenous midazolam (slow infusion) and

one placebo tablet, 30 minutes before receiving ketamine as an anesthesia. Thirty minutes after receiving this intervention, patients are receiving 1-2 mg/kg intravenous ketamine during 30-60 seconds and then receiving 0.25-0.5 mg/kg intravenous ketamine every 10 minutes as a maintenance dose (maximum 5 mg/kg).

Category

Treatment - Drugs

2

Description

Intervention group 2: In this group patients are receiving 0.3 mg/kg oral melatonin and 2 ml intravenous placebo (distilled water), 30 minutes before receiving ketamine as an anesthesia. Thirty minutes after receiving this intervention, patients are receiving 1-2 mg/kg intravenous ketamine during 30-60 seconds and then receiving 0.25-0.5 mg/kg intravenous ketamine every 10 minutes as a maintenance dose (maximum 5 mg/kg).

Category

Treatment - Drugs

3

Description

Control group: In this group patients are receiving one oral placebo tablet and 2 ml intravenous placebo (stilled water), 30 minutes before receiving ketamine as an anesthesia. Thirty minutes after receiving this intervention, patients are receiving 1-2 mg/kg intravenous ketamine during 30-60 seconds and then receiving 0.25-0.5 mg/kg intravenous ketamine every 10 minutes as a maintenance dose (maximum 5 mg/kg).

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center
Alzahra hospital
Full name of responsible person
Saeed Majidinejad
Street address
Alzahra hospital, Sofe Street, Isfahan City
City
Isfahan
Province
Isfehan
Postal code
8174675731
Phone
+98 31 3620 2020
Email
Saeedmajidinejad@yahoo.com

2

Recruitment center

Name of recruitment center
Kashani hospital
Full name of responsible person
Saeed Majidinejad
Street address
Kashani hopital, Kashani Street, Isfahan City
City
Isfahan
Province
Isfehan
Postal code
8183983434
Phone
+98 31 3233 0091
Email
saeedmajidinejad@yahoo.com

Sponsors / Funding sources

1

Sponsor

Name of organization / entity
Esfahan University of Medical Sciences
Full name of responsible person
Shaghayegh Haghjou Javanmard
Street address
Isfahan University of Medical Science, Hezarjrib Street, Isfahan City
City
Isfahan
Province
Isfehan
Postal code
8174673461
Phone
+98 31 3668 0048
Email
sh_haghjoo@med.mui.ac.ir

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
Mehdi Botshekan

Position
Resident

Latest degree
Specialist

Other areas of specialty/work
Emergency Medicine

Street address
Isfahan University of Medical Science, Hezarjrib Street, Isfahan CIty

City
Isfahan

Province
Isfehan

Postal code
8174673461

Phone
+98 31 3668 0048

Email
saeedmajidinejad@yahoo.com

Person responsible for scientific inquiries

Contact

Name of organization / entity
Esfahan University of Medical Sciences

Full name of responsible person
Saeed Majidinejad

Position
Associate Professor

Latest degree
Specialist

Other areas of specialty/work
Emergency Medicine

Street address
Isfahan University of Medical Science, Hezarjrib Street, Isfahan City

City
Isfahan

Province
Isfehan

Postal code
8174673461

Phone
+98 31 3668 0048

Email
saeedmajidinejad@yahoo.com

Person responsible for updating data

Contact

Name of organization / entity
Esfahan University of Medical Sciences

Full name of responsible person
Saeed Majidinejad

Position
Associate Professor

Latest degree
Specialist

Other areas of specialty/work
Emergency Medicine

Street address
Isfahan University of Medical Science, Hezarjrib Street, Isfahan City

City
Isfahan

Province
Isfehan

Postal code
8174673461

Phone
+98 31 3668 0048

Email
saeedmajidinejad@yahoo.com

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
Not applicable

Informed Consent Form
No - There is not 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
Not applicable

Data Dictionary
Not applicable