Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

A Comparative Study on the Efficacy of Amitriptyline and Melatonin in the Preventive Treatment of Migraine in Children referred to Imam Hossain Hospital in 20205

Protocol summary

Study aim

The aim of this study is to evaluate the efficacy and tolerability of melatonin compared to amitriptyline in the prevention of migraine headaches in children aged 5 to 15 years who presented with recurrent migraine to the pediatric neurology clinic of Imam Hossein Hospital during the year 2025.

Design

This study is a randomized, single-blind, parallel-group clinical trial designed to compare the efficacy and tolerability of melatonin versus amitriptyline for migraine prevention in children aged 5 to 15 years

Settings and conduct

The study will be conducted at the Pediatric Neurology Clinic of Imam Hossein Hospital, affiliated with Isfahan University of Medical Sciences. Eligible children visiting the clinic during 2025 (1404) will be enrolled after obtaining informed consent. Participants will be randomized into melatonin and amitriptyline groups using block randomization. The intervention will last for 12 weeks, with biweekly follow-up visits conducted by a pediatric research assistant.

Participants/Inclusion and exclusion criteria

Inclusion Criteria: Children aged 5–15 years with migraine (with/without aura) per ICHD-II, ≥1 attack/week, PedMIDAS >10, and no prior prophylactic treatment. Exclusion Criteria: Secondary headache, systemic illness, drug allergy, epilepsy or complicated migraine, psychiatric disorders, >4 analgesic doses/week, prior prophylaxis (except study meds), or lack of consent.

Intervention groups

Intervention Group 1: Melatonin Children in this group will receive oral melatonin 3 mg once nightly for a duration of 12 weeks. Intervention Group 2: Amitriptyline Children in this group will receive oral amitriptyline at a dose of 1 mg/kg once nightly for a duration of 12 weeks.

Main outcome variables

•Monthly frequency of migraine attacks •Headache severity (based on Visual Analog Scale) •Migraine-related disability score (PedMIDAS)

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20250517065765N1**
Registration date: **2025-07-20, 1404/04/29**
Registration timing: **retrospective**

Last update: **2025-07-20, 1404/04/29**
Update count: **0**

Registration date

2025-07-20, 1404/04/29

Registrant information

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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

2025-05-13, 1404/02/23

Expected recruitment end date

2025-06-14, 1404/03/24

Actual recruitment start date

empty

Actual recruitment end date
empty
Trial completion date
empty

Scientific title
A Comparative Study on the Efficacy of Amitriptyline and Melatonin in the Preventive Treatment of Migraine in Children referred to Imam Hossain Hospital in 20205

Public title
A study on the effects of melatonin and amitriptyline on the severity and frequency of migraine headaches in children
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
1.Age between 5 and 15 years 2.Diagnosis of migraine headache (with or without aura) based on the second edition of the International Classification of Headache Disorders (ICHD-II), confirmed by a pediatric neurologist 3.Experiencing at least one headache episode per week 4.Having moderate to severe migraine-related disability, defined as a PedMIDAS score >10 5.No use of any migraine prophylactic medications prior to enrollment in the study
Exclusion criteria:
1.Children with secondary headaches or systemic diseases (e.g., renal or hepatic failure, cardiac, hematologic, or endocrine disorders), based on physical examination and paraclinical findings (e.g., lab tests or neuroimaging if increased intracranial pressure is suspected) 2.Children or parents unwilling to participate in the study 3.Children with a history of drug allergy 4.Children with epilepsy or complex migraine 5.Children showing severe and uncontrolled adverse effects to melatonin or amitriptyline 6.Children receiving other migraine prophylactic drugs (except melatonin or amitriptyline) 7.Children with migraine and significant psychiatric comorbidities (e.g., depression or ADHD) who use analgesics more than 4 times per week
Age
From **5 years** old to **15 years** old
Gender
Both

Phase
3
Groups that have been masked

- Outcome assessor
- Data analyser

Sample size
Target sample size: **60**
Randomization (investigator's opinion)
Randomized
Randomization description
Block randomization will be used, with 14 blocks of 4 participants each. The randomization process will be performed by a researcher not involved in the clinical management of participants. Both participants and the nurse administering the medication will be aware of group assignment, but the data analyst will remain blinded. Medications will be pre-coded, packed, and labeled prior to the study. At the time of assignment, the nurse will provide the medication package to the pediatric neurologist, who will calculate the appropriate dosage based on the child's weight. Outcome assessment will be performed by a research assistant who is blinded to group allocation.
Blinding (investigator's opinion)
Single blinded
Blinding description
In this study, only the outcome assessor and the data analyst are blinded. Medications are pre-coded and packed by an independent individual before the study begins. Clinical assessments are performed by a research assistant who is unaware of the treatment allocation. Data will also be provided to the statistician without group identifiers to ensure blinded statistical analysis.
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Research Ethics Committee of Isfahan University of Medical Sciences
Street address
No. 2, Sahar Alley, Western Omid Street, Mahfarrokhi Square, Khaneh Isfahan, Isfahan, Iran
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Isfehan
Postal code
8139965573
Approval date
2025-05-12, 1404/02/22
Ethics committee reference number
IR.MUI.MED.REC.1404.078

Health conditions studied

1

Description of health condition studied
Recurrent migraine headaches in children aged 5 to 15 years
ICD-10 code
G43.0, G43
ICD-10 code description
Migraine without aura [common migraine] ,Migraine with

aura [classical migraine]

Primary outcomes

1

Description
Number of migraine attacks per month before and after the intervention
Timepoint
Outcome variables will be measured at baseline (before intervention) and then every two weeks during the 3-month treatment period
Method of measurement
The number of migraine attacks will be recorded daily by the parents and children in a headache diary. Additionally, headache intensity will be assessed using the Numerical Rating Scale (NRS), and headache-related disability will be evaluated by the Pediatric Migraine Disability Assessment Scale (PedMIDAS) during biweekly visits. All data will be collected and recorded by a trained research assistant.

Secondary outcomes

1

Description
Headache Frequency
Timepoint
Every 2 weeks during the 3-month treatment period
Method of measurement
Number of headache attacks recorded daily by parents and child in a headache diary.

2

Description
Headache Severity
Timepoint
Every 2 weeks at each visit
Method of measurement
Headache severity assessed using Numeric Rating Scale (NRS) or Visual Analog Scale (VAS)

3

Description
Headache Disability (pedMIDAS)
Timepoint
At baseline and at the end of the 3-month treatment period
Method of measurement
Disability assessed by the Pediatric Migraine Disability Assessment Score (pedMIDAS) questionnaire

4

Description
Analgesic Use
Timepoint
Throughout the treatment period
Method of measurement
Number of days the child used analgesics recorded in the diary

5

Description
Drug Side Effects
Timepoint
Every 2 weeks at each visit
Method of measurement
Side effects recorded through parent reports and clinical examinations

6

Description
Treatment Response
Timepoint
At the end of the 3-month treatment period
Method of measurement
More than 50% reduction in monthly headache frequency considered as good response

Intervention groups

1

Description
Group 1: Oral melatonin at a dose of 0.3 mg/kg (maximum 6 mg) once daily before bedtime for 90 days
Category
Treatment - Drugs

2

Description
Intervention group: Oral amitriptyline at a dose of 1 mg/kg (maximum 50 mg) once daily before bedtime for 90 days
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Pediatric Neurology Clinic, Imam Hossein Children’s Hospital, Isfahan University of Medical Sciences
Full name of responsible person
Dr Neda Hosseini Meshkani
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Sponsors / Funding sources

1

Sponsor
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Full name of responsible person
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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
No
Title of funding source
Part of the study expenses are funded by Isfahan University of Medical Sciences (Vice Chancellor for Research). The remaining expenses are self-funded.
Proportion provided by this source
40
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
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Sharing plan

Deidentified Individual Participant Data Set (IPD)
No - There is not a plan to make this available
Justification/reason for indecision/not sharing IPD
Due to the sensitive nature of the collected data, ethical considerations, and strict adherence to participant privacy and confidentiality, as advised by the Ethics Committee, individual participant data (IPD) will not be shared.
Study Protocol
No - There is not a plan to make this available
Statistical Analysis Plan
No - There is not a plan to make this available
Informed Consent Form
No - There is not a plan to make this available
Clinical Study Report
No - There is not a plan to make this available
Analytic Code
No - There is not a plan to make this available
Data Dictionary
No - There is not a plan to make this available