

Clinical Trial Protocol

Iranian Registry of Clinical Trials

11 Sep 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

Name

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Name of organization / entity

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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

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No. 2, Sahar Alley, Western Omid Street, Mahfarrokhi Square, Khaneh Isfahan, Isfahan, Iran

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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