

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

25 Jun 2026

### Effect of prophylactic caffeine on the sleep/wake cycles (SWC) in preterm neonates with RDS treated with nasal CPAP with a gestational age of 28-35 weeks.

#### Protocol summary

##### Study aim

We will investigate the effect of caffeine on the sleep-wake cycle (SWC) in neonates with gestational age of 28-35 weeks with respiratory distress syndrome (RDS) requiring nasal CPAP (nCPAP) by using amplitude-integrated EEG (aEEG).

##### Design

This study is a single blinded interventional randomized controlled clinical trial phase 3 with two parallel groups (17 neonates in each group). They will randomly allocate by permutation random block method with blocks of 4 in two groups of caffeine treatment (F) and control group (C).

##### Settings and conduct

The study will be conducted in the neonatal intensive care unit at shahid-beheshti hospital in Isfahan, Iran. The eligible infants randomly assigned to caffeine and control groups since birth. After 48 hours of birth, the sleep-wake cycles of neonates in both groups will be monitored by aEEG for 24 hours.

##### Participants/Inclusion and exclusion criteria

Inclusion criteria include neonates with gestational age of 28-35 weeks and spontaneous breathing who are under nCPAP support due to RDS. Exclusion criteria are infants who have perinatal asphyxia; congenital brain anomalies; evidence of Patent Ductus Arteriosus (PDA) in echocardiography; evidence of intraventricular Hemorrhage (IVH) grade III or IV in cranial ultrasonography; existence of air leak; tachycardia (HR more than 180 beat/min) during study and neonates who do not need nCPAP after 48 hours of birth.

##### Intervention groups

The eligible infants will be randomly assigned into two groups of caffeine (F) or control (C). Infants in the F group received 20 mg/kg caffeine as the initial dose since birth, and then it will continue with 10 mg/kg daily as the maintenance dose until discontinuation of nCPAP

and oxygen administration. Infants in the C group will not receive any placebo or similar drugs.

##### Main outcome variables

The effect of caffeine on the number and duration of sleep-wake cycle of neonate.

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20170627034782N3**

Registration date: **2022-07-06, 1401/04/15**

Registration timing: **prospective**

Last update: **2022-07-06, 1401/04/15**

Update count: **0**

##### Registration date

2022-07-06, 1401/04/15

##### Registrant information

##### Name

Ramin Iranpour

##### Name of organization / entity

Isfahan University of Medical Sciences

##### Country

Iran (Islamic Republic of)

##### Phone

+98 31 3386 8247

##### Email address

iranpour@med.mui.ac.ir

##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2022-09-23, 1401/07/01

##### Expected recruitment end date

2023-03-20, 1401/12/29

**Actual recruitment start date**

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

Effect of prophylactic caffeine on the sleep/wake cycles (SWC) in preterm neonates with RDS treated with nasal CPAP with a gestational age of 28-35 weeks.

**Public title**

Effect of prophylactic caffeine on the sleep/wake cycles (SWC) in preterm neonates.

**Purpose**

Diagnostic

**Inclusion/Exclusion criteria**

**Inclusion criteria:**

Preterm neonate with a gestational age of 28-35 weeks, Spontaneous breathing with clinical sign and symptom of RDS requiring nasal CPAP.

**Exclusion criteria:**

Perinatal Asphyxia ( apgar score fifth minute=0-3, umbilical cord PH<7, umbilical cord bicarbonate <12 meq/l), Evidence of PDA which is confirmed by echocardiography, Evidence of IVH ( grade 3-4) which is confirmed by cranial sonography, Existence of air leakage, Neonate with congenital brain anomaly, Neonate with tachycardia (heart rate >180), Neonate not requiring nasal CPAP till 48 hours after birth.

**Age**

From **1 day** old to **1 day** old

**Gender**

Both

**Phase**

3

**Groups that have been masked**

- Participant

**Sample size**

Target sample size: **34**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

The study sample was randomly allocated by permutation random block method with blocks of 4 in two groups of caffeine treatment (F) and control group (C).

**Blinding (investigator's opinion)**

Single blinded

**Blinding description**

Only neonates participating in the study are not aware of the drug prescription.

**Placebo**

Not 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 Sciences, Isfahan, Iran

**Street address**

Research deputy, Isfahan University of Medical Sciences, Hezarjerib Blvd.

**City**

Isfahan

**Province**

Isfahan

**Postal code**

8184757851

**Approval date**

2022-07-02, 1401/04/11

**Ethics committee reference number**

IR.MUI.MED.REC.1401.145

**Health conditions studied**

**1**

**Description of health condition studied**

The effect of caffeine in quantity and quality of sleep/wake cycle in newborns by using of aEEG

**ICD-10 code**

**ICD-10 code description**

**Primary outcomes**

**1**

**Description**

The number of sleep-wake cycle during of one 24 hour

**Timepoint**

From 48 hours after birth till 24 hour later continuously.

**Method of measurement**

Brain monitoring with amplitude Electroencephalography (aEEG)

**Secondary outcomes**

**1**

**Description**

apnea of prematurity

**Timepoint**

24 hour cardio-respiratory monitoring

**Method of measurement**

pulse oximeter with Spo2 continuous monitoring

**2**

**Description**

The mean duration of active phase of sleep

**Timepoint**

From 48 hours after birth till 24 hour later continuously.

**Method of measurement**

Brain monitoring with amplitude Electroencephalography (aEEG).

**3**

**Description**

The mean duration of quiet phase of sleep.

**Timepoint**

From 48 hours after birth till 24 hour later continuously.

**Method of measurement**

Brain monitoring with amplitude Electroencephalography (aEEG).

**4**

**Description**

The mean heart rate.

**Timepoint**

Every 6 hour, since birth till 72 hour after birth

**Method of measurement**

Cardio-respiratory monitoring by pulse oximeter.

**5**

**Description**

The mean arterial oxygen saturation.

**Timepoint**

Every 6 hour, since birth till 72 hour after birth

**Method of measurement**

Every 6 hour, since birth till 72 hour after birth

**6**

**Description**

chronic lung disease

**Timepoint**

Daily

**Method of measurement**

Physical exam and chest xray

**Intervention groups**

**1**

**Description**

Intervention group: In the caffeine group (F), the premature neonates with a gestational age of 28- 35 weeks with RDS and requiring nCPAP will be receive 20 mg/kg caffeine as the initial dose since birth, and then it will continue with 10 mg/kg daily as the maintenance dose until discontinuation of nCPAP and oxygen administration. After 48 hours of birth, the sleep-wake cycles of neonates will be monitored by aEEG for 24 hours.

**Category**

Diagnosis

**2**

**Description**

Control group: In the control group (C), the premature neonates with a gestational age of 28- 35 weeks with RDS and requiring nCPAP will be will not receive any placebo or similar drugs. After 48 hours of birth, the sleep-wake cycles of neonates will be monitored by aEEG for 24 hours.

**Category**

Diagnosis

**Recruitment centers**

**1**

**Recruitment center**

**Name of recruitment center**

shahid-Beheshti Hospital, Isfahan

**Full name of responsible person**

Ramin Iranpour

**Street address**

No.16, Sout Resalat St., Mardavij Ave.

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**Postal code**

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iranpour@med.mui.ac.ir

**Web page address**

<https://mui.ac.ir>

**Sponsors / Funding sources**

**1**

**Sponsor**

**Name of organization / entity**

Esfahan University of Medical Sciences

**Full name of responsible person**

Dr Mansour Siavash Dastjerdi

**Street address**

Hezar-jerib street, Isfahan University of Medical Sciences, Deputy of research and technology Building number 4,

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research@mui.ac.ir

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**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**

Dr Ramin Iranpour

**Position**

Neonatologist/Associate Professor

**Latest degree**

Subspecialist

**Other areas of specialty/work**

Pediatrics

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## Person responsible for scientific inquiries

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**Position**

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**Latest degree**

Subspecialist

**Other areas of specialty/work**

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## Person responsible for updating data

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**Full name of responsible person**

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**Position**

Associate professor of Pediatrics in Isfahan Medical Faculty

**Latest degree**

Subspecialist

**Other areas of specialty/work**

Pediatrics

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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**

There is no further information.

**Study Protocol**

No - There is not 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