Clinical Trial Protocol
Iranian Registry of Clinical Trials

11 Jul 2026

Comparing the efficacy of inhaled versus infused milrinone in management of persistent pulmonary hypertension(PPHN) in infants

Protocol summary

Study aim
Comparison of the efficacy of inhaled and injectable milrinone in the treatment of PPHN

Design
the parallel-group randomized trial, one-sided blinding, phase 3 on 32 patients, block randomization, randomization of blocks through random number table

Settings and conduct
Infants admitted to the NICU with PPHN are randomly divided into two groups, after considering inclusion and non-inclusion criteria. Demographic information, maternal underlying diseases, vital signs, and clinical findings are recorded in the checklist. Both groups receive an intravenous dopamine infusion, then the control and intervention groups receive intravenous milrinone and inhaled milrinone respectively، until the patient recovers or develops symptoms of respiratory distress or increased oxygen demand Echocardiography is repeated in the first 24 hours of hospitalization, 24 hours after the start of treatment, and when the infant shows signs of respiratory distress or increased oxygen demand (by a physician unaware of the treatment task). Rhythm, PR, intravascular pressure, urinary output, peripheral perfusion, and IV injection site are controlled. In the event of hypotension, arrhythmia, HR> 220, and thrombocytopenia, the infant is excluded from the study, and supportive measures are initiated for the infant.

Participants/Inclusion and exclusion criteria
entry: Infants 1 to 28 days with a diagnosis of PPHN; Hospitalized in NICU and indicated for treatment; Existence of conscious parental consent No entry: Neonates with congenital heart disorders, diaphragmatic hernias, pulmonary abnormalities; Infants are candidates for major surgery to eliminate abnormality

Intervention groups
1: Dopamine + injectable milrinone 2: Dopamine + inhaled milrinone

Main outcome variables
Pulmonary artery pressure, Systemic artery pressure, Symptoms of respiratory distress, Oxygen supply index, Die or survive

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20220130053890N1**
Registration date: **2022-02-26, 1400/12/07**
Registration timing: **prospective**

Last update: **2022-02-26, 1400/12/07**
Update count: **0**

Registration date
2022-02-26, 1400/12/07

Registrant information

Name
Peyman Shahhosseini

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
2022-03-01, 1400/12/10

Expected recruitment end date
2022-11-21, 1401/08/30

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
Comparing the efficacy of inhaled versus infused milrinone in management of persistent pulmonary hypertension(PPHN) in infants

Public title
milrinone in persistent neonatal pulmonary hypertension

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Infants 1 to 28 days with a diagnosis of persistent pulmonary hypertension (diagnosed on Basis of echocardiographic findings) and hospitalization in the NICU. Indicated for receiving treatment based on the diagnosis of the treating physician. Existence of informed consent of parents to enter the study.

Exclusion criteria:
Neonates with congenital heart disorders, diaphragmatic hernias, pulmonary abnormalities. infants are candidates for major surgery to eliminate abnormality.

Age
From **1 day** old to **28 days** old

Gender
Both

Phase
3

Groups that have been masked

- Outcome assessor

Sample size
Target sample size: **32**

Randomization (investigator's opinion)
Randomized

Randomization description
Randomization with blocks, using binary blocks, Randomization of blocks using random number table. The intervention and control groups are called A and B, respectively, we prepare two series of blocks No. 1 (AB) and No. 2 (BA). Select a point in the table of random numbers at random and start moving in one direction. In each cell of the table, if the digit is an odd number, select block 1, and if it is even, selects block two, and place it in a row until 16 blocks selected (based on sample size). Then, each eligible patient who entered the study will be placed in the intervention or control group according to the order obtained.

Blinding (investigator's opinion)
Single blinded

Blinding description
The patient's echocardiography is performed by a different pediatrician who is unaware of the type of treatment intervention.

Placebo
Not used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics committee of Iran University of Medical Sciences

Street address
No. 174, Mozaffarikhah St., North Kargar St., Tehran

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Tehtan

Province
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Postal code
1413654591

Approval date
2021-11-21, 1400/08/30

Ethics committee reference number
IR.IUMS.FMD.REC.1400.493

Health conditions studied

1

Description of health condition studied
neonatal

ICD-10 code

ICD-10 code description

Primary outcomes

1

Description
Pulmonary artery pressure: pulmonary artery pressure greater than 40 mm Hg is considered PPHN.

Timepoint
it is measured at first, during the first 24 hours of hospitalization, 24 hours after the start of treatment, and when the infant shows signs of respiratory distress or increased oxygen demand.

Method of measurement
Pulmonary artery pressure is determined by M-mode, two-dimensional, and color-Doppler echocardiography using the Bernoulli formula. Bernoulli equation: pulmonary artery systolic pressure (PASP) = tricuspid regurgitation gradient + right atrial pressure (RAP), PASP = (Vmax2 × 4) + RAP

2

Description
Systemic artery pressure: Systolic and diastolic blood pressure

Timepoint
daily

Method of measurement

Using the NICU monitoring device

3

Description
signs of respiratory distress: Respiratory distress in the newborn is recognized as one or more signs of increased work of breathing, such as tachypnea, nasal flaring, chest retractions, or grunting
Timepoint
The baby is constantly monitored.
Method of measurement
Through clinical examination of the patient

4

Description
Oxygenation index(OI) : is used to assess the severity of hypoxic respiratory failure (HRF) and persistent pulmonary hypertension of the newborn (PPHN)
Timepoint
Daily and at the time of respiratory distress
Method of measurement
It is calculated by the following formula: (OI=mean airway pressure MAP × FiO2 × 100÷PaO2)

Secondary outcomes

1

Description
Die or survive
Timepoint
During treatment
Method of measurement
See the patient

Intervention groups

1

Description
Intervention group: treated with intravenous infusion of dopamine at a dose of 5 macro per kg body weight per minute for 3 to 5 days according to the doctor and then receive inhaled milrinone at a rate of 50 micrograms per kilogram body weight, during For 10 minutes with a frequency of twice a day. the intervention continues until the symptoms improve or the symptoms of respiratory distress or the need for oxygen increase.
Category
Treatment - Drugs

2

Description
Intervention group: Treated with intravenous infusion of dopamine at a dose of 5 macro per kg of infant weight per minute for 3 to 5 days according to the doctor's opinion and then, continuous injection of 0.3 to 0.5 micrograms per kg of body weight per minute Milrinone as a continuous intravenous infusion. the intervention continues until the symptoms improve or the symptoms of respiratory distress or the need for oxygen increase.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Hazrat Ali Asghar hospital
Full name of responsible person
peyman shahhosseini
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Iran University of Medical Sciences
Full name of responsible person
Hossein keyvani
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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
Iran 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
Iran University of Medical Sciences
Full name of responsible person
peyman shahhosseini
Position
fellow of neonatology
Latest degree
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Other areas of specialty/work
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Person responsible for updating data

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

Data Dictionary	Not applicable