Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

The effect of early oral probiotics prescription on feeding intolerance, regain birth weight and secondary outcomes in very low birth weight (VLBW) infants

Protocol summary

Study aim

The effect of early oral probiotics prescription on feeding intolerance, regain birth weight and secondary outcomes in very low birth weight infants.

Design

Two blinded randomized clinical trial with control group, phase 3 on 300 very low birth weight neonates. Stratify Block Randomization is used for randomization. Function rand of Microsoft Excel would be used For randomization.

Settings and conduct

This study will be performed in the neonatal intensive care unit of Mahdieh Hospital in Tehran. This study evaluated the early administration of oral probiotics on feeding intolerance, incidence of sepsis, incidence of necrotizing enterocolitis and length of hospital stay in these infants. Infants are continuously checked by special checklist designed by the researcher. For blinding, placebo drops are used in front of drug drops with the same packaging, with non-sequential and indistinguishable coding for people who do not have access to the key. The parents of the baby, the doctor or the nurse prescribing the medicine are blinded.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Hospitalization in neonatal intensive care unit, Born weight less than 1500 gr, Stable hemodynamic status, Ability to enteral nutrition, Parent's written consent. Exclusion criteria: Dissatisfaction of parents, Unstable clinical status.

Intervention groups

In this study, very low birth weight infants placed in two groups of intervention and control randomly and the intervention from the first day of birth at the first 2 hours and once daily, before or after milk feeding and for 14 days in the groups. In the intervention group, probiotic is prescribed 5 drops per day and the placebo is prescribed in control group that Contains maltodextrin which is quite similar to the drug in terms of color, smell and taste and it is 5 drops too.

Main outcome variables

Feeding intolerance

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20220505054746N1**
Registration date: **2022-08-04, 1401/05/13**
Registration timing: **prospective**

Last update: **2022-08-04, 1401/05/13**
Update count: **0**

Registration date

2022-08-04, 1401/05/13

Registrant information

Name

Fatemeh Heydari

Name of organization / entity

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2022-08-23, 1401/06/01

Expected recruitment end date

2024-08-22, 1403/06/01

Actual recruitment start date

empty

Actual recruitment end date
empty
Trial completion date
empty

Scientific title
The effect of early oral probiotics prescription on feeding intolerance, regain birth weight and secondary outcomes in very low birth weight (VLBW) infants

Public title
The effect of early oral probiotics prescription in very low birth weight (VLBW) infants
Purpose
Prevention
Inclusion/Exclusion criteria
Inclusion criteria:
Hospitalization in NICU ward Born weight less than 1500 gr Stable hemodynamic status Ability to enteral nutrition Parent's written consent
Exclusion criteria:
Dissatisfaction of parents Impossibility of starting standard nutrition for neonate Existence of any congenital anomalies in neonate Neonate's CPR need in labor room Unstable clinical status Being a child of mothers with substance abuse disorders Severe abdominal distension or peptic hemorrhage Immunodeficiency in the family of neonate Congenital enteral perforation or atresia Complete forbidding of oral feeding
Age
From **1 day** old to **2 days** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Care provider

Sample size
Target sample size: **300**
Randomization (investigator's opinion)
Randomized
Randomization description
In order to homogenize the patients in terms of the intervening variables of mechanical ventilation (invasive-non-invasive) and type of nutrition (breast milk-formula) and to create a balance in the number of samples allocated to each of the studied groups, sampling method was used by random sampling. It is stratified block randomization. So that before starting the study, we first adjust the number of floors based on different levels of two qualitative variables. In this study, we will have 4 floors as follows. First class: patients who have aggressive ventilation and breast milk feeding. Second class: patients who have non-invasive ventilation and breast milk feeding. Third class: patients who have non-invasive ventilation and formula nutrition. Fourth class: patients who have aggressive ventilation and formula nutrition. We consider the sample size of each tier to be 75 to achieve a sample size of 300. For each class separately, we perform randomized block sampling. We consider the capacity of the blocks as 4 and then we write all the possible permutations for this block, which are defined as follows. (1: ABAB) and (2: AABB) and (3: BBAA) and (4: BABA) and (5: ABBA) and (6: BAAB) By means of a dice, we choose one of the numbers 1 to 6 and consider the corresponding block. For example, if the first random selection of block 5 is selected, the first person will receive treatment A, the second and third persons will receive treatment B, and the fourth person will receive treatment A. To reach a sample size of 75 per stratum, we continue this process 19 times. After selecting all the blocks, we randomly assign index A to one of the treatment groups. At the end, we merge the samples of all classes together and use the total sample for analysis.
Blinding (investigator's opinion)
Double blinded
Blinding description
The placebo drop is used against the drug with the same packaging, with non -sequential coding for people who do not have access to the key. Parents of the neonate and doctor or indicator nurse have been blinded and will be contacted by the original researcher if needed, and at the end of the study and completion of the questionnaires, they will be identified by the code.
Placebo
Used
Assignment
Other
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Ethics committee of Shahid Beheshti University of Medical Sciences
Street address
Shahid Beheshti University of Medical Sciences, Velenjak Blvd., Tehran, Iran.
City
Tehran
Province
Tehran
Postal code
1985717443
Approval date
2022-02-06, 1400/11/17
Ethics committee reference number
IR.SBMU.RETECH.REC.1400.1068

Health conditions studied

1

Description of health condition studied
Very Low Birth Weight
ICD-10 code
P07.0
ICD-10 code description
Extremely low birth weight newborn

2

Description of health condition studied
1_2.499 weight
ICD-10 code
P07.1
ICD-10 code description
Other low birth weight newborn

3

Description of health condition studied
feeding intolerance
ICD-10 code
P92.5
ICD-10 code description
Neonatal difficulty in feeding at breast

4

Description of health condition studied
Abdominal distension
ICD-10 code
ICD-10 code description
P14

5

Description of health condition studied
vomiting
ICD-10 code
ICD-10 code description
P11

6

Description of health condition studied
Digestive bleeding
ICD-10 code
ICD-10 code description
P54.3

7

Description of health condition studied
necrotic enterocolitis
ICD-10 code
ICD-10 code description
P77

8

Description of health condition studied
Sepsis
ICD-10 code
ICD-10 code description
P36.9

Primary outcomes

1

Description
Feeding intolerance
Timepoint
In each feeding time
Method of measurement
Checklist

Secondary outcomes

1

Description
Sepsis
Timepoint
Daily
Method of measurement
Based on having clinical and specific symptoms of sepsis (including irritability of the baby, rapid breathing or apnea, changes in the skin color of the baby, diarrhea, poor sucking, poor feeding) and positive result of blood culture and CRP result recorded in the checklist in daily evaluations.

2

Description
Necrotic Enterocolitis
Timepoint
Daily
Method of measurement
Based on having clinical and specific symptoms of Necrotizing Enterocolitis (including lethargy, increased volume of food residue, bloody or bilious vomiting, ileus, persistent abdominal distension, bloody stools, symptoms of peritonitis and shock) and the Bells scale, which is evaluated in the checklist designed by the researcher.

3

Description
Time of hospitalization
Timepoint
Daily
Method of measurement
Checklist

4

Description
Time to reach total nutrition
Timepoint
Daily
Method of measurement
The days required to reach enteral nutrition of 100

milliliter per kilogram per day are evaluated with the checklist made by the researcher.

5

Description
Reach to born weight
Timepoint
Daily
Method of measurement
The weight of the infant will be assessed in terms of grams (in grams) until the clinical condition stabilizes and then daily until the day of discharge from the hospital. At the end of the weighting process, each premature infant will be assessed using Fenton growth charts. All measurements will be performed with a digital scale for fixed infants with the help of a researcher and will be recorded in a checklist created by the researcher.

Intervention groups

1

Description
Intervention group: early administration of oral probiotics in infants with very low birth weight. In this study, infants with very low birth weight from the first day of birth in the first 24 hours and once a day, before or after feeding with milk (in breastfeeding intervals) and for 14 days in the probiotic intervention group (containing Bifidobacterium lactis 3 5*100000000 colony forming units (CFU) and Bifidobacterium infantis 3.5*100000000 CFU and Streptococcus thermophilus 3*100000000 CFU) which is prepared in 700 mg sachets with maltodexerin and is 5 drops per day. It should be mentioned that this product is made by Farabiotic company.
Category
Prevention

2

Description
Control group: administration of placebo in babies with very low birth weight. In this study, babies with very low birth weight from the first day of birth, in the first 24 hours and once a day, before or after feeding with milk (in breastfeeding intervals) and for 14 days in the control group, placebo (containing maltodextrin, which is The color, smell and taste are completely similar to the medicine) which is prepared in 700 mg sachets and is prescribed in the amount of 5 drops. It should be mentioned that this product is made by Farabiotic Company.
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Mahdiyeh Educational Hospital
Full name of responsible person
Naeeme Taslimi Taleghani
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Shahid Beheshti University of Medical Sciences
Full name of responsible person
Afshin Zarghi
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Next to Taleghani Hospital,Shahid Arabi Street,Yemen Street, Shahid Chamran Highway,
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Email
info@sbmu.ac.ir
Grant name
Research Assistant of Shahid Beheshti University of Medical Sciences
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Shahid Beheshti 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
Shahid Beheshti University of Medical Sciences
Full name of responsible person
Fatemeh Heydari
Position
Pediatric Instructor
Latest degree
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Other areas of specialty/work
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Person responsible for updating data

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Other areas of specialty/work
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Province
Qazvin
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3415843899
Phone
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Email
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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is a plan to make this available
Study Protocol
Yes - There is a plan to make this available
Statistical Analysis Plan
Yes - There is a plan to make this available
Informed Consent Form
Yes - There is a plan to make this available
Clinical Study Report
Yes - There is a plan to make this available
Analytic Code
Yes - There is a plan to make this available
Data Dictionary
Yes - There is a plan to make this available
Title and more details about the data/document
The main outcomes will be available.
When the data will become available and for how long
Six months after publishing.
To whom data/document is available
The data will be available per request for people working in academic institutions.
Under which criteria data/document could be used
The data will available for using in systematic review and meta-analysis.
From where data/document is obtainable
The data will be available by contacting email: naeemetaslimi@yahoo.com.
What processes are involved for a request to access data/document
The data will available for using in systematic review and meta-analysis.
Comments