

Clinical Trial Protocol

Iranian Registry of Clinical Trials

10 Jul 2026

Comparison of prophylactic effect of synbiotic on necrotizing enterocolitis, sepsis and hyperbilirubinemia with placebo on very low birth weight infants

Protocol summary

Summary

Objective: Prebiotics are synergistic with probiotics and enhance survival probiotic bacteria in human milk. The goal of this study was to investigate the efficacy of synbiotic preparation in preventing necrotizing enterocolitis, sepsis, and hyperbilirubinemia in very low birth weight infants. Design: A prospective, double blinded, randomized, placebo controlled trial. Setting: Single center in Istanbul, Turkey. Patients: Infants (n: 220) were born ≤ 32 gestational age, ≤ 1500 g birth weight. Interventions: Very low birth weight infants who started enteral feeding were randomized either to receive daily feeding supplementation with synbiotic (NBL ATP 1/2 sachet every 12 hours) or placebo until discharge. The sample was randomized via computer centre. Main outcome measures: Necrotizing enterocolitis (Bell's stage ≥ 2), sepsis, and hyperbilirubinemia.

General information

Acronym

IRCT registration information

IRCT registration number: **IRCT2013062710279N3**
Registration date: **2015-01-18, 1393/10/28**
Registration timing: **retrospective**

Last update:

Update count: **0**

Registration date

2015-01-18, 1393/10/28

Registrant information

Name

Ozge Serce Pehlevan

Name of organization / entity

Zeynep Kamil Maternity and Children Education and

Training Hospital

Country

Turkey

Phone

08 60 193 612 0900

Email address

ozge.serce@marmara.edu.tr

Recruitment status

Recruitment complete

Funding source

NBL Pharmacy

Expected recruitment start date

2012-10-01, 1391/07/10

Expected recruitment end date

2013-10-01, 1392/07/09

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Comparison of prophylactic effect of synbiotic on necrotizing enterocolitis, sepsis and hyperbilirubinemia with placebo on very low birth weight infants

Public title

Outcome of synbiotics on necrotizing enterocolitis, sepsis

Purpose

Prevention

Inclusion/Exclusion criteria

Inclusion criteria: Very low birth weight infants (gestational age: ≤ 32 weeks; birth weight: ≤ 1500 g) who survived to feed enterally (minimum age: first postnatal day, maximum age: 10 days). Exclusion criteria: Infants who had severe asphyxia (stage III), major congenital anomalies, those who had been fasted for more than 3

weeks, died within the first postnatal 14 days.

Age

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

Gender

Both

Phase

3

Groups that have been masked

No information

Sample size

Target sample size: **210**

Randomization (investigator's opinion)

Randomized

Randomization description

Blinding (investigator's opinion)

Double blinded

Blinding description

Placebo

Used

Assignment

Parallel

Other design features

The event rate was determined by unpublished data based on 2009–2010 of our NICU. Our recent event rate for NEC or sepsis was 31% and for death or NEC was 35% in our NICU (for NEC alone 17%, for sepsis alone 19%, and for death alone 18%). With the α -error set at 0.05 and the β -error set at 0.2, and an absolute reduction in the incidence of either NEC/sepsis or NEC/death of 50%, the number of infants needed to verify our hypothesis was 104 for NEC or sepsis and 92 for NEC or death for each group. The infants enrolled in the study were assigned randomly to the intervention or control group prospectively after informed parental consent was obtained. Randomization was performed by using sequential numbers generated at the computer center.

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ministry of Health of Turkey, General Directorate of Pharmaceuticals and Pharmacy

Street address

No 5, 2176 Sok., Söğütözü Mah.

City

Ankara

Postal code

06520

Approval date

2012-07-20, 1391/04/30

Ethics committee reference number

17

Health conditions studied

1

Description of health condition studied

Necrotizing enterocolitis

ICD-10 code

p77

ICD-10 code description

Necrotizing enterocolitis of fetus and newborn

2

Description of health condition studied

Sepsis

ICD-10 code

P36

ICD-10 code description

Bacterial sepsis of newborn

3

Description of health condition studied

Hyperbilirubinemia

ICD-10 code

P59.3

ICD-10 code description

Neonatal jaundice from breast milk inhibitor

Primary outcomes

1

Description

Necrotizing enterocolitis

Timepoint

Starts at the same time with the intervention

Method of measurement

Patients' medical records

2

Description

Sepsis

Timepoint

Starts at the same time with the intervention

Method of measurement

Patients' medical records

3

Description

Hyperbilirubinemia

Timepoint

Starts at the same time with the intervention

Method of measurement

Serum sample

Secondary outcomes

1

Description

Weight gain per week

Timepoint

Starts on the 7th day of intervention

Method of measurement

Patients' medical records

2

Description

Time to reach full enteral feeding

Timepoint

Starts at the same time with the intervention

Method of measurement

Patients medical records

3

Description

Mortality until hospital discharge

Timepoint

Starts at the same time with the intervention

Method of measurement

Patients' medical records

4

Description

Length of hospitalization

Timepoint

Starts at the same time with the intervention

Method of measurement

Patients' medical records

5

Description

Neurocognitive development

Timepoint

18 months corrected age

Method of measurement

Bayley test

Intervention groups

1

Description

The intervention group received synbiotic preparation (Probiotic ATP, NBL, 1/2 sachet per dose twice daily) which were added to breast milk or formula until discharge.

Category

Treatment - Drugs

2

Description

The control group received placebo (distilled water; 1 cc per dose twice daily) which were added to breast milk or formula until discharge.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Zeynep Kamil Maternity and Children's Education and Training Hospital

Full name of responsible person

Fahri Ovalı

Street address

No:3-4, Dr.Burhanettin Üstünel Sokak , Zeynep Kamil Mahallesi,

City

Istanbul

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

NOBEL Pharmacy

Full name of responsible person

Emre Bulbun

Street address

No:10, Akçakoca Sok., İnkılap mah.

City

Istanbul

Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

NOBEL Pharmacy

Proportion provided by this source

Public or private sector

empty

Domestic or foreign origin

empty

Category of foreign source of funding

empty

Country of origin

Type of organization providing the funding

empty

2

Sponsor

Name of organization / entity

Ministry of Health of Turkey, General Directorate of Pharmaceuticals and Pharmacy

Full name of responsible person

Cem Razi

Street address

No:5, 2176. Sok., Söğütözü Mah.

City

Ankara

Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Ministry of Health of Turkey, General Directorate of Pharmaceuticals and Pharmacy
Proportion provided by this source
Public or private sector
empty
Domestic or foreign origin
empty
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
empty

Person responsible for general inquiries

Contact

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Zeynep Kamil Maternity and Children's Education and Training Hospital
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Sharing plan

Deidentified Individual Participant Data Set (IPD)

empty
Study Protocol
empty
Statistical Analysis Plan
empty
Informed Consent Form
empty
Clinical Study Report
empty
Analytic Code
empty
Data Dictionary
empty