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
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Turkey
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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., Inkılap 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

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Web page address

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