

Clinical Trial Protocol

Iranian Registry of Clinical Trials

27 Jul 2026

Comparison of prophylaxis effect of *Saccharomyces boulardii* on necrotizing enterocolitis with placebo on very low birth weight infants

Protocol summary

Summary

Objective: The efficacy and safety of probiotics are controversial in preterm infants. They have strain specific effects and the effects of fungi have been investigated poorly. The goal of this study was to investigate the efficacy of *Saccharomyces boulardii* in preventing necrotizing enterocolitis and sepsis in very low birth weight infants. Design: A prospective, double blinded, randomized, placebo controlled trial. Setting: Single center in Istanbul, Turkey. Patients: Infants 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 probiotic (*Saccharomyces boulardii* 50 mg/kg every 12 hours) or placebo until discharge. Main outcome measures: Necrotizing enterocolitis (Bell's stage ≥ 2) and sepsis.

General information

Acronym

IRCT registration information

IRCT registration number: **IRCT2012071410279N1**

Registration date: **2012-10-19, 1391/07/28**

Registration timing: **retrospective**

Last update:

Update count: **0**

Registration date

2012-10-19, 1391/07/28

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

Drug was insured from Biocodex.

Expected recruitment start date

2010-10-01, 1389/07/09

Expected recruitment end date

2011-11-30, 1390/09/09

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Comparison of prophylaxis effect of *Saccharomyces boulardii* on necrotizing enterocolitis with placebo on very low birth weight infants

Public title

Outcome of *Saccharomyces boulardii* prophylaxis on necrotizing enterocolitis

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: 1 week). 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 and infants who used antifungal therapy were excluded.

Age

To **1 year** old

Gender
Both

Phase
3

Groups that have been masked
No information

Sample size
Target sample size: **208**

Randomization (investigator's opinion)
Randomized

Randomization description

Blinding (investigator's opinion)
Double blinded

Blinding description

Placebo
Used

Assignment
Parallel

Other design features
Patients were assigned randomly to the study or control group by the principal investigator. Randomization was performed by using sequential numbers generated at the computer center. Feeding nurse who was not involved in the care of the infants added *Saccharomyces boulardii* to the feeding. She gave the feeding without label to the nurse who was responsible from the infant's care. The first investigator who randomized patients and ordered supplementation to the feeding nurse gave just only the patients name to the second investigator for follow-up. Therefore, the only personnel who knew the infants' group assignments were the first investigator and the feeding nurse, who were not involved in the care of the study infants.

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Health Ministry Drug and Pharmacy General
Management

Street address

Söğütözü Mahallesi 2176. Sokak No:5

City

ANKARA

Postal code

06520

Approval date

2010-09-23, 1389/07/01

Ethics committee reference number

08

Health conditions studied

1

Description of health condition studied

Necrotizing enterocolitis, neonatal sepsis

ICD-10 code

P77, P36

ICD-10 code description

Necrotizing enterocolitis of fetus and newborn, bacterial sepsis of newborn

Primary outcomes

1

Description

Sepsis

Timepoint

Starts at the same time with the intervention

Method of measurement

Patients' medical records

2

Description

Necrotizing enterocolitis

Timepoint

Starts at the same time with the intervention

Method of measurement

Patients' medical records

Secondary outcomes

1

Description

Length of hospitalization

Timepoint

Starts at the same time with the 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

Weight gain per week

Timepoint

Starts on the 7th day of 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 study group received *Saccharomyces boulardii* (Reflor®, Biocodex, France, 50 mg/kg 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 Education and Training Hospital

Full name of responsible person

Fahri Ovalı

Street address

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

City

Istanbul

Sponsors / Funding sources

1

Sponsor**Name of organization / entity**

Health Ministry Drug and Pharmacy General Management

Full name of responsible person

Saim KERMAN

Street address

Söğütözü Mahallesi 2176. Sokak No:5

City

Ankara

Grant name**Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

Title of funding source

Health Ministry Drug and Pharmacy General Management

Proportion provided by this source

100

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****Name of organization / entity**

Zeynep Kamil Maternity and Children Education and Training Hospital

Full name of responsible person

Guner Karatekin

Position

Clinical Chief

Other areas of specialty/work**Street address**

Neonatal intensive care unit-1

City

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ÜSKÜDAR

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Web page address**Person responsible for scientific inquiries****Contact****Name of organization / entity**

Zeynep Kamil Maternity and Children Education and Training Hospital

Full name of responsible person

Fahri Ovalı

Position

Professor, Clinical chief

Other areas of specialty/work**Street address**

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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

Person responsible for updating data**Contact****Name of organization / entity**

Zeynep Kamil Maternity and Childen Education and
Training Hospital

Full name of responsible person

Ozge Serce

Position

Specialist in neonatology

Other areas of specialty/work**Street address**

Zeynep Kamil Mahallesi, Dr.Burhanettin Üstünel