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Evaluation of the synbiotic Prodefen GG drops in pediatric patients with acute diarrhea of probable viral etiology

Submission date
17/07/2024

Recruitment status
No longer recruiting

Registration date
28/08/2024

Overall study status
Completed

Last Edited
17/07/2024

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims.
Acute viral gastroenteritis is a very common illness in healthy children worldwide. Little children and their caregivers must cope with several days of unpleasant diarrhea till full recovery. Recent studies have shown the efficacy of probiotics in the improvement of diarrhea.
This study objective is to assess clinical benefit of a new liquid formulation of a multistrain synbiotic (probiotics+prebiotics) over standard measures (diet and/or oral rehydration) for the management of acute diarrhea of probable viral origin in infants.

Who can participate?
Infants aged 2 years or younger, with acute diarrhea of less than 48 hours of evolution.

What does the study involve?
The present randomized controlled trial, PRODINFANT study, was designed to assess the effectiveness of a multistrain synbiotic compound in a new drops formulation for treating Acute Gastroenteritis of viral origin in a group of children in the first 2 years of life. Patients were randomized in 2 groups in order to receive a 7-day treatment of a 7-multistrain synbiotic drops in addition to supportive therapy (Synbiotic group) or supportive therapy (diet and/or oral rehydration) alone (Control group). The objective of the study is to evaluate the additional benefits of the synbiotic therapy to treat acute diarrhea in children over standard supportive measures.

What are the possible benefits and risks of participating?
There are risks associated with any treatment intervention; however regarding to probiotics, this risk is low. Randomized clinical trials have examined the safety of probiotics and have shown that they are well tolerated and associated with few adverse events in healthy individuals at doses higher than those used in the current study. Some of the adverse events reported in previous studies with probiotics included rash, nausea, gas, flatulence, abdominal bloating, abdominal pain, vomiting, increased phlegm, chest pain, constipation, taste alteration, and loss of appetite.
The microorganisms contained in Prodefen GG drops are considered probiotics and therefore

are usually part of the host's intestinal microbiota. For these reasons, we can consider it a safe product.
Probiotics are effective in the prevention and management of various diseases, especially those directly related to the human intestine, including acute diarrhea of possible viral etiology or antibiotic-associated diarrhea (AAD). Therefore, we can consider that the study is conducted according to usual clinical practice.
For the children in the treated group, a benefit is assumed, as a reduction in the duration of diarrhea is expected due to the action of the dietary supplement Prodefen GG drops.
For the control group receiving only the standard treatment of diet and oral rehydration, participation in this study will not represent any additional benefit.

Where is the study run from?
The study will be run from 10 pediatric primary care consultations or emergency services throughout Spain.

When is the study starting and how long is it expected to run for?
July 2018 to July 2022

Who is funding the study?
ITF RESEARCH PHARMA S.L.U. (Spain)

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Protocol serial number
RES-6066-C1

Study information

Scientific Title
Effectiveness of a multistrain synbiotic product in children with acute viral diarrhea: a multicenter prospective randomized controlled study

Acronym
PRODINFANT

Study objectives
To assess the clinical benefit of a new liquid formulation of a multistrain synbiotic (probiotics+prebiotics) over standard measures (diet and/or oral rehydration) for the management of acute diarrhea of probable viral origin in infants.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/11/2018, Clinical Research Ethics Committee (CEIC) of Hospital Universitario Puerta de Hierro (C/ Joaquín Rodrigo, 2, Madrid, 28222, Spain; +34 91 191 60 00; secreceic.hpth@salud.madrid.org), ref: 19.18

Primary study design
Interventional

Study design
Multicenter prospective randomized open-label and controlled clinical trial

Study type(s)
Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Acute diarrhea of probable viral etiology

Interventions
PRODINFANT study is designed as a multicenter, prospective, randomized, open-label and controlled clinical trial. A cohort of children presenting an acute diarrhea will be randomized between two groups, Synbiotic Group will receive a one-week treatment with a 7-multistrain synbiotic drops in addition to supportive therapy and Control Group will be assigned to supportive therapy (diet and/or oral rehydration) alone.
Investigators belong to pediatric primary care consultations or emergency services throughout Spain.

Children who met the inclusion criteria will be assigned a consecutive number at each study site according to the order of arrival, and then randomized to treatment with the synbiotic product (synbiotic group; odd number) or standard supportive measures (control group; even number). All participants regardless of their assigned group receive supportive standard treatment with diet and/or oral rehydration therapy. Children randomized to the synbiotic group receive a daily recommended dosage (10 drops) of the synbiotic product (Prodefen® drops, ITALFARMACO, S. A., Alcobendas, Madrid, Spain), with or without food and preferably in the morning for 7 consecutive days.

The study includes a 7-day treatment period with 3 visits (1 in-person visit and 2 visits by phone) and a final safety follow-up phone call at day 10. Children visiting the study center (visit 1) will be assigned to the treatment group, after inclusion criteria is confirmed, and signed informed consent is obtained. The first dose of the synbiotic product will be administered by the investigator at the study center (day 1) and parents are provided with a drop bottle of the product for treatment during the subsequent 6 days. Parents of all participants are given a patient diary card in which all information of the study variables have to be recorded on a daily basis. The parents are contacted by phone on days 4 and 7, so that the investigator can collect information on the study variables related to the course of the disease. Data of acceptability and tolerability of treatment are collected on day 7. In addition, on day 10, 3 days after the end of the treatment, adverse events occurring during that period will be recorded. If scheduled phones calls are foreseen during the weekend, a 2-day window period will be allowed.

Intervention Type
Supplement

Primary outcome(s)
Efficacy is measured using the percentage of children who suffer diarrhea according to several definitions, the WHO criteria, the Bristol Stool Form Scale (BSFS) criteria, both WHO and BSFS criteria, and the parents' opinion regarding more stools per day or more fluid in consistency for at least 1, ≥2 or ≥3 consecutive days from day 1 to the end of the study

Key secondary outcome(s)
1. Number of days of diarrhea (three or more passage of stools per day) and duration (days) of diarrhea are measured until the end of the study
2. Recovery is measured by the percentage of children recovered from diarrhea (2 consecutive days without diarrhea) and the stool characteristics (frequency, consistency according to the BSFS, severity of diarrhea) throughout the study
3. Associated symptoms (vomiting, nausea, fever, mucus in stools and abdominal pain) are measured by the duration of symptoms and need of treatment throughout the study
4. Recovery are measured counting the number of visits to the primary care pediatrician or the emergency service as well as the need of concomitant medication throughout the study
5. Tolerability of the synbiotic product and satisfaction with treatment (acceptability) are measured using a 5-point Likert scale, from "very good" to "very bad" and from "very satisfied" to "not at all satisfied", respectively at week 8
6. The impact of treatment on the quality of life and daily activities of the parents will be assessed using a 5-point Likert scale from "not at all affected" to "extremely affected" at week 4 and 8

Completion date
08/07/2022

Eligibility

Key inclusion criteria
1. Children from both sex whose parents/guardians have given their informed consent to participate in the study
2. Children aged 2 years or younger who visited the pediatrician in the primary or the emergency healthcare center, presenting an acute diarrhea episode lasting less than 48 hours, with a probable viral origin
3. Children whose diarrhea will be treated only with diet and/or oral rehydration, on an

outpatient basis
4. Children for whom the pediatrician considers treatment with the dietary supplement Prodefen GG drops as an additional treatment measure

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
0 Years

Upper age limit
2 Years

Sex
All

Total final enrolment
75

Key exclusion criteria
1. Children who have presence of any disease that may cause diarrhea, different from an infection, such as inflammatory bowel disease, food allergy, lactose intolerance, etc.
2. Immunocompromised children, children with valve implants, and/or those with a history of infectious endocarditis, due to the risk of bacteremia
3. Children with severe dehydration or malnutrition
4. Children with visible blood in stools
5. Children with current pharmacological treatment for diarrhea
6. Children who have used antibiotics and/or probiotics the previous 7 days
7. Children allergic to milk protein (Prodefen GG drops may contain traces of milk, but do not affect those who are lactose intolerant)
8. Children currently participating in another study
9. Children allergic to any of the components of Prodefen GG drops

Date of first enrolment
01/09/2020

Date of final enrolment
26/11/2021

Locations

Countries of recruitment
Spain

Study participating centre
Centro medico privado-MEDInfant
Barcelona
Spain
08022

Study participating centre
Hospital Vigen del Mar
Madrid
Spain
28016

Study participating centre
Hospital Público Universitario del Sureste
Arganda del Rey
Spain
28500

Study participating centre
HBN 39 Especialidades Médicas
Madrid
Spain
28036

Study participating centre
Centro Medico Oporto
Madrid
Spain
28025

Study participating centre
Hospital Quiron A Coruña
A Coruña
Spain
15009

Study participating centre

Consultorio Pediatrico Dr. Hugo Daniel Ruiz Morena
San Sebastián de los Reyes, Madrid
Spain
28701

Study participating centre
Centro Médico Valdebernardo, S.L.P.
Madrid
Spain
28032

Study participating centre
Madrid Pediátrica Consultas
Madrid
Spain
28016

Study participating centre
Consultorio Privado
Madrid
Spain
28042

Sponsor information

Organisation
ITF RESEARCH PHARMA S.L.U.

Funder(s)

Funder type
Industry

Funder Name
ITF RESEARCH PHARMA S.L.U.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to sponsor product patent requirements, as well as preserving participants sensitive data protection.

IPD sharing plan summary
Not expected to be made available