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Efficacy and safety of a probiotic supplement containing L. plantarum and P. acidilactici strains in young children with common respiratory viral infections

Submission date 04/10/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 05/10/2023	**Overall study status** Completed	
Last Edited 28/08/2024	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Uncomplicated upper respiratory infections are common in children and typically caused by viruses. Previous studies have shown intake of some probiotics can reduce the duration of such respiratory infections in children, when taken in a preventive manner. The aim of this study is to determine if a particular probiotic formula can reduce the duration of symptoms when taken after the onset of such respiratory infections in children.

Who can participate?
Infants and children, 6 months to 5 years old, with an upper respiratory infection with fever and throat pain (pharyngitis), whose symptoms are of likely viral origin, as per doctor's judgment.

What does the study involve?
Eligible children are randomly allocated to receive either the specific probiotic formula (containing strains L. plantarum KABP033, KABP023 and KABP022 and P. acidilactici KABP021) in capsules, or identically-looking placebo capsules, twice daily. Study subjects can also receive standard of care treatment, at study investigators discretion, consisting of ibuprofen (an approved anti-inflammatory drug) and/or cetirizine (an approved anti-histaminic drug).

Parents or caregivers are taught to rate their children's pain using a visual scale (the FLACC scale). Parents or caregivers are instructed to fill a daily diary with the observed FLACC score, as well as the highest body temperature, presence of runny nose (rhinorrhea), nasal congestion, cough, use of ibuprofen and use of cetirizine.

What are the possible benefits and risks of participating?
The probiotic strains used in this study were previously found to be safe, as well as effective at shortening the duration of fever and respiratory symptoms in a clinical trial in 300 Covid19 patients. Therefore, children who participate in this study could have the duration of the symptoms of their upper respiratory infection shortened. And if an adverse health event

occured related to the participation in the study, the participants can reach the investigators anytime (24h availability by phone every day), and costs would be covered by an insurance already contracted by the study funder.

Where is the study run from?
Medica Sur Hospital, in Mexico City. (Mexico)

When is the study starting and how long is it expected to run for?
May 2023 to September 2024

Who is funding the study?
AB-BIOTICS SA (part of KANEKA Corporation) (Spain)

Who is the main contact?
Dr Diana Maria Andrade Platas, dianamandrade@yahoo.com

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Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
RESPIKIDS-II

Study information

Scientific Title
Efficacy and safety of L. plantarum KABP033, KABP023 and KABP022 and P. acidilactici KABP021 in upper respiratory tract infections of viral origin in children aged 6 months to 5 years

Study objectives
The combination of probiotic strains L. plantarum KABP033, KABP023 and KABP022 and P. acidilactici KABP021, when taken twice daily, would reduce the duration of symptoms of upper respiratory tract infections of viral origin, compared to placebo.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 22/09/2023, Commitee for Ethics and Research in Studies in Humans (Comité de Ética e Investigación para Estudios en Humanos (CEIEH)), Medica Sur Hospital (Puente de Piedra No. 150 Colonia Toriello Guerra, Tlalpan, Mexico City, 14050, Mexico; +52 55 5424 7200; comiteinvestigacion@medicasur.org.mx), ref: CB148-CEI153

Study design
Randomized double-blind placebo-controlled parallel-group study

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request participant information sheet

Health condition(s) or problem(s) studied
Upper respiratory tract infections with pharyngitis, of likely viral origin, in children 6 months to 5 years old

Interventions
Using a centralised computer-based randomisation list, patients are randomised 1:1 to receive either probiotic capsules or indentical-looking placebo capsules, to be taken orally twice daily for 15 days (days 1 to 15 of the study). Randomisation list will be prepared by personnel not directly participating in the study and kept in a sealed enveloppe until study completion.

Probiotic capsules contain Lactoplantibacillus plantarum strains KABP033, KABP023 and KABP022 and Pediococcus acidilactici strain KABP021, totaling 2 billion CFUs (colony-forming units) in a dextrin carrier. Placebo capsules contain dextrin carrier only. All capsules are made of hydroxymethyl-propyl-cellulose (HPMC) and are delivered in anonymous blisters, inside of anonymous boxes (30 capsules per box).

Study subjects can also receive pediatric standard of care treatment, at study investigators discretion, consisting of ibuprofen suspension as anti-inflammatory drug (10mg per Kg of body weight per day) and/or cetirizine suspension as anti-histaminic drug (0.25mg per Kg of body weight per day). Finally, should study subjects develop infectious symptoms of likely bacterial origin after the study initiation, study investigators can prescribe antibiotic rescue medication at standard pediatric doses, consisting of amoxicillin clavulanate suspension (at 45mg per Kg of body weight per day), or clarythromycin suspension (at 7.5 mg per Kg of body weigh per day) if there is a history of allergy to penicillins.

Intervention Type
Supplement

Primary outcome measure
Numer of days with fever (body temperature >37.5°C), as measured with a thermometer, and number of days with pain score >3, as measured with the FLACC score ("Face, Legs, Activity, Cry and Consolability"; Merkel et al. Pediatric Nursing 1997, 23:293-297), both recorded daily by parents in a diary from day 1 to 15 of intervention.

Secondary outcome measures

1. Area under the curve (AUC) of the FLACC score ("Face, Legs, Activity, Cry and Consolability"; Merkel et al. Pediatric Nursing 1997, 23:293-297), as recorded daily by parents in a diary from day 1 to 15 of intervention.
2. Area under the curve (AUC) of body temperature (in Celsius degrees), as recorded daily by parents in a diary from day 1 to 15 of intervention.
3. Etiological agent (using multiplex PCR for 16 respiratory viruses), as determined on nasopharyngeal swabs taken on day 0.
4. Metabolome analysis (polar and semi-polar metabolites, as analysed by HPLC-MS) of salivary samples taken on days 1 and 15.
5. Concentration of immunoglobulin A (IgA), TNF-alpha and interleukins 1b, 4, 6, 10, 17 and 18 in salivary samples taken on days 1 and 15.
6. Number of days with cough, as recorded daily by parents in a diary from day 1 to 15 of intervention.
7. Number of days with nasal congestion, as recorded daily by parents in a diary from day 1 to 15 of intervention.
8. Number of days with rhinorrhea, as recorded daily by parents in a diary from day 1 to 15 of intervention.
9. Number of days of intake of NSAIDs (ibuprofen), as recorded daily by parents in a diary from day 1 to 15 of intervention.
10. Number of days of intake of antihistaminics (cetirizine), as recorded daily by parents in a diary from day 1 to 15 of intervention.
11. Number of days of intake of antibiotics rescue medication, as recorded daily by parents in a diary from day 1 to 15 of intervention.
12. Number of medical or emergency visits, as recorded daily by parents in a diary from day 1 to 15 of intervention.
13. Number of medical or emergency visits after day 15, as recorded during face-to-face visits on days 30 and 60.
14. Number of different symptoms (of FLACC>3, fever >37.5ºC, presence of cough, rhinorrhea and nasal congestion), as recorded daily by parents in a diary from day 1 to 15 of intervention.
15. Number of different symptoms (of FLACC>3, fever >37.5ºC, presence of cough, rhinorrhea and nasal congestion), as recorded during face-to-face visits on days 30 and 60.

Overall study start date
02/05/2023

Completion date
20/09/2024

Eligibility

Key inclusion criteria
1. Infants and children, 6 months to 5 years old, with upper respiratory infection of likely viral origin (based on investigator's judgment of symptoms) with pharyngitis.
2. Having a FLACC score ("Face, Legs, Activity, Cry and Consolability"; Merkel et al. Pediatric Nursing 1997, 23:293-297) > 3 and body temperature >37.5ºC.
3. Symptoms started within 48h of entry visit.
4. Written informed consent provided by parents or caregivers.

Participant type(s)
Patient

Age group
Child

Lower age limit
6 Months

Upper age limit
5 Years

Sex
Both

Target number of participants
90

Total final enrolment
75

Key exclusion criteria
1. Tonsillitis, cervical lymphadenitis, otitis media or scarlatiniform rash (symptoms suggestive of bacterial infection).
2. Preterm infants or those having been born weighting <2500gr.
3. Failure to thrive
4. Use of antibiotics, antivirals or probiotics for more than 48h within 2 weeks of study entry.
5. Breastfed children whose mothers have taken antibiotics, antivirals or probiotics for more than 48h within 2 weeks of study entry.
6. History of two or more invasive infections (meningitis, osteomielitis, sepsis).
7. History of recurrent, severe respiratory infections within 12 months of study entry
8. Chronic diarrhea or gastroesophagic reflux disease (GERD).
9. Congenital heart, respiratory or digestive disease.
10. Primary or secondary immunodeficiency.
11. Asthma.
12. Any other condition that, according to the judgment of the principal investigator, warrants exclusion from the study

Date of first enrolment
14/10/2023

Date of final enrolment
15/12/2023

Locations

Countries of recruitment
Mexico

Study participating centre
Medica Sur Hospital
Puente de Piedra No. 150 Colonia Toriello Guerra, Tlalpan

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Sponsor information

Organisation
AB-BIOTICS SA (KANEKA Corp.)

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Industry

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Funder(s)

Funder type
Industry

Funder Name
AB-BIOTICS SA (KANEKA Corp.)

Results and Publications

Publication and dissemination plan
Study results will be submitted for presentation(s) at primary care and/or pediatric medicine conference(s), and for publication in international peer-reviewed scientific journal(s).

Intention to publish date
31/12/2024

Individual participant data (IPD) sharing plan

After publication, individual anonymised participant data generated during and/or analysed during the current study will be available upon request from: Jordi Espadaler-Mazo, PhD. (espadaler@ab-biotics.com)

IPD sharing plan summary

Available on request