Study Identification

Protocol ID: IRESP.PROB

Brief Title

"Clinical trial to evaluate the efficacy of a probiotic preparation in the prevention of upper respiratory tract infections in adults".

Official Title

"Randomized, double-blind, placebo-controlled clinical trial to evaluate the efficacy of a probiotic preparation in the prevention of upper respiratory tract infections in a healthy adult population".

Study Status

Study Start

First patient included: 16/10/2023.

Study Completion

End of the follow-up period of the last included patient: 27/02/2024

Results and completion: 30/06/24

Sponsor/Collaborators

Sponsor: Centro Sperimentale del Latte S.r.l

Collaborators: MiBioPath Research Group – UCAM

Ethics Committee

Board Affiliation: Ethics Committee of the Catholic University San Antonio de Murcia (UCAM).

Approval number: CE092303 – 29/09/2023

Study Description

Brief Summary

Randomized, double-blind, placebo-controlled, parallel-group, clinical trial to assess the efficacy of the intake of a probiotic product composed of *Lacticaseibacillus rhamnosus* CRL1505 strain in reducing or preventing upper respiratory tract infections (URTIs) in a healthy adult population.

Keywords: prevention, upper respiratory tract infections, probiotics, microbiota, microbiome

Description

Randomized, double-blind, placebo-controlled, parallel-group, clinical trial.

The study aims to demonstrate the efficacy of the intake of a probiotic product composed of *Lacticaseibacillus rhamnosus* CRL1505 strain in reducing or preventing upper respiratory tract infections in a healthy adult population.

The study will be focused on a healthy population, so the exclusion criteria will rule out individuals with major acute or chronic illnesses and an immunocompromised state. In addition, those subjects with a regular pharmacological treatment or consumption of food supplements that could influence the outcome of the study in the last 4 weeks prior to inclusión will be excluded. If patients could discontinue this treatment after a washout period and during the intervention period, they would be able to participate in the study. However, the usual medication that is considered not to influence the results of the study will be allowed. Subjects recently vaccinated against influenza will also be excluded, but as the study focuses on a healthy population, a priori vaccination is not recommended and there would be no problem in finding subjects with these characteristics because there is no contradiction.

In addition, subjects included will be asked not to modify their diet or physical activity during the study.

An important data that is not usually recorded in many studies is the use of medication to alleviate the symptoms of URTI, either non-prescription or prescribed by the physician. Only antibiotic medication to treat or prevent bacterial upper respiratory tract coinfections or complications is usually established as a variable (the use of antibiotics is established as a secondary variable in the present study). We consider that it is very important to record the use of these treatments to evaluate if any study group is unbalanced in this regard and/or whether it is a confusion factor when interpreting the results. We could consider the possibility of performing a post hoc analysis of this topic and present it in the final report if the results are interesting.

Similarly, it is important to collect baseline data related to the type of work or continuous contact with people with risk factors such as children or elderly to assess whether the groups are balanced. It will also be collected data about the number of URTIs in the study subjects since 3 months prior to inclusion.

The treatment period will be 12 weeks. There will then be a follow-up period (without treatment) of 4 weeks to evaluate the sustained effect of the probiotic product. The study will be structured in 3 face-to-face visits at week 0, 12 and 16.

For the evaluation of the efficacy variables, a diary would be provided to the study subject for a daily evaluation. Saliva collection kits for the determination of salivary IgA in the initial o final visits will also be provided.

The complete inclusion process will be carried out in October and November so that the study was located in the months of highest URTI incidence.

Study Design

Study type: Interventional

Interventional Study Model: Randomized, double-blind, placebo-controlled with parallel assignment

Number of arms: 2

Masking: Double (Participant and Investigator)

Allocation: Randomized

Enrollment: 140 patients

Arms and Interventions

Experimental arm

Probiotic group: Probiotic product containing *Lacticaseibacillus rhamnosus* CRL1505 formulated in a vegetable hydroxymethylpropyl-cellulose capsule of size 2. Test product is a food supplement and not an investigational medicinal product.

Placebo comparator

Placebo group: Placebo product containing cornstarch, in a vegetable hydroxymethylpropyl-cellulose capsule of size 2.

Outcome measures

Primary Outcome Measure

- Number of URTIs, with the following endpoints:
    - Difference in the proportion of patients who were diagnosed with at least 1 URTI during the intervention period between the study groups.
    - Difference in the proportion of patients who were diagnosed with at least 2 URTIs during the intervention period between the study groups.
    - Difference in the total number of URTIs between the study groups during the intervention period.
    - Difference in the average number of URTIs per participant between the study groups during the intervention period.
    - Same evaluations, but referring to the different URTIs detected, mainly the common cold and influenza.
    - Same evaluations but referred after a follow-up period (16 weeks).

Secondary Outcome Measures

- Difference in the proportion of participants who presented URTI complications such as pneumonia, otitis media and acute sinusitis during intervention and follow-up periods between study groups.
- Difference in the number of URTI complications such as pneumonia, otitis media and acute sinusitis during intervention and follow-up periods between study groups.
- Difference in first URTI time (days), URTI mean period (days), URTI-free rate (%) during intervention and follow-up periods between study groups.

- Difference in the proportion of participants who presented gastrointestinal infections intervention and follow-up periods between study groups.
- Difference in the number of gastrointestinal infections intervention and follow-up periods between study groups.
- Difference in mean salivary IgA concentrations during intervention period between study groups.
- Difference in the proportion of participants using antibiotics during intervention and follow-up periods between study groups.
- Difference in the days with antibiotics treatment during intervention and follow-up periods between study groups.
- Difference in the proportion of participants using symptomatic treatment during intervention and follow-up periods between study groups.
- Difference in the days with symptomatic treatment during intervention and follow-up periods between study groups.
- Difference in mean “common cold episode day” WURSS-21 score during intervention and follow-up periods between study groups.

Safety Variables

- Incidence and severity of all Adverse Events.
- Incidence of Severe Adverse Events.
- Incidence and severity of Adverse Events related to the study product.
- Incidence and severity of Adverse Events leading to study withdrawal.
- Rate of withdrawal due to intolerance to study product.

Eligibility

Inclusion Criteria

- Healthy men and women between 18 and 65 years.
- Signed Informed Consent to participate in the study.
- BMI less than 35 kg/$m^{2.}$

Exclusion Criteria

- Chronic pathological conditions such as chronic respiratory diseases (asthma, chronic bronchitis, chronic obstructive pulmonary disease etc), chronic heart diseases (chronic heart failure etc), chronic neurological diseases (Parkinson´s diseases, multiple esclerosis etc), chronic liver diseases, kidney liver diseases, gastrointestinal diseases, hematologic disorders etc, or other disease or condition that the researcher considers.
- Metabolic disorders (diabetes, obesity with BMI greater than 35.1 kg/m^2 etc).

- Congenital or acquired immune defects (including allergies).
- Immunocompromised individuals (HIV infection, chemotherapy, post-trasplant, chronic corticosteroid treatment etc).
- Presence of nasal ulcers/nasal polyps or other conditions that could cause nasal obstruction.
- Abuse of alcohol, tobacco or other drugs.
- Pregnancy or lactation.
- Regular intake of products that could influence the study outcome (immune suppressants/immune stimulants including paramedication such as Echinacea, analgesics, antiinflammatories, antitussives/expectorants, influenza remedies, mouth or throat therapeutics, decongestants, antibiotics, antihistaminergic drugs, probiotics) within the last 4 weeks prior to the study start.
- Influenza vaccination in the last 6 monts.

Withdrawal Criteria

- Loss of tracking

- Withdrawal of consent

- Lack of collaboration

- Any pathological situation that develops during the study and at the investigator's discretion does not allow it to continue

- Suffering an Adverse Event that prevents them from performing the study procedures or complying with the study treatments.

- Use of other probiotics during the study

- Treatment adherence less than 85%

Locations

Catholic University of Murcia (UCAM). MiBioPath Research Group

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