Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

The Use of Streptococcus salivarius K12 in treatment of Periodic fever with aphthous stomatitis, pharyngitis, and adenitis (PFAPA) Syndrome

Protocol summary

Study aim

Determination of the effectiveness of the probiotic Streptococcus salivarius K12 in the treatment of patients with Periodic fever , aphthous stomatitis, pharyngitis, and adenitis (PFAPA) Syndrome

Design

Clinical trial with control group, with parallel groups, three-arm blind, randomized, phase 2 on 30 patients. This will be done using the random block method using the site sealedenvelop.com.

Settings and conduct

in this study, children with a diagnosis of PFAPA referred to the rheumatology and allergy clinic of Akbar Children's Hospital in Mashhad are divided into two groups.one group receive lactogam and other group get plasebo

Participants/Inclusion and exclusion criteria

Inclusion criteria: All patients under 18 who are diagnosed with PFAPA based on the Marshall Crater by a pediatric rheumatologist. Non-entry conditions: 1-Parents' dissatisfaction to participate in the project, 2-All patients with overlap syndrome

Intervention groups

In this randomized trial study, patients with a diagnosis of PFAPA based on Marshall Crater will be divided into two groups. . In one group, in addition to the previously used therapies, lactogam therapy (manufactured by Zist Takhmiir Company), which contains the probiotic Streptococcus salivarius K12($>10^9$CFU), should be used by the patient as a suction for 4 months and at night before going to bed. The other group (control) under previous standard treatments will include acetaminophen and the NSAID prednisolone. A placebo will also be used in this group (control) where the placebo will be similar in shape and color to the intervention group. The method of prescribing it will be the same.

Main outcome variables

Evaluation of the number of disease attacks in case and control groups, Investigating the distance between the incidence of attacks in the case and control groups, Determining the change in the number of symptoms in attacks in the case group

General information

Reason for update

Acronym

PFAPA

IRCT registration information

IRCT registration number: **IRCT20210911052436N1**
Registration date: **2021-11-27, 1400/09/06**
Registration timing: **registered_while_recruiting**

Last update: **2021-11-27, 1400/09/06**
Update count: **0**

Registration date

2021-11-27, 1400/09/06

Registrant information

Name

Nafiseh pourbadakhshan

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone

+98 51 3859 6431

Email address

pourbadakhshann@mums.ac.ir

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2021-09-01, 1400/06/10

Expected recruitment end date

2022-09-01, 1401/06/10

Actual recruitment start date

empty

Actual recruitment end date
empty
Trial completion date
empty

Scientific title
The Use of Streptococcus salivarius K12 in treatment of Periodic fever with aphthous stomatitis, pharyngitis, and adenitis (PFAPA) Syndrome

Public title
Evaluation of the effect of probiotics on periodic fever
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
All patients under 18 who are diagnosed with PFAPA based on the Marshall Cratria by a pediatric rheumatologist.
Exclusion criteria:
1-Dissatisfaction of parents to participate in the project ,2-All patients with overlap syndrome
Age
From **1 month** old to **18 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Outcome assessor
- Data analyser

Sample size
Target sample size: **30**
Randomization (investigator's opinion)
Randomized
Randomization description
Block Randomization will be performed using the quadratic block method. A random sequence based on quadratic blocks will be generated by the design methodologist using the sealedenvelope.com website. The sequence produced in sealed envelopes will be opaque and sealed and then numbered sequentially. The person allocating the samples will open the envelopes in order after fulfilling the entry conditions of the participants.
Blinding (investigator's opinion)
Triple blinded
Blinding description
blinding (study subjects, evaluators, analysts) Due to the use of placebo in the control group, participants will be blinded to the study group. Outcome assessment will be performed by a person separate from the patient's therapist and this person will not be aware of the assigned groups. The data are specified in groups a and b at the time of analysis and the data analyst will be unaware of the intervention and control group.
Placebo
Used
Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Ethics committee of Mashhad University of Medical Sciences
Street address
Namaz Blvd , Akbar hospital
City
Mashhad
Province
Razavi Khorasan
Postal code
9166655688
Approval date
2021-08-31, 1400/06/09
Ethics committee reference number
IR.MUMS.MEDICAL.REC.1400.408

Health conditions studied

1

Description of health condition studied
Periodic fever with aphthous stomatitis, pharyngitis, and adenitis
ICD-10 code
R50
ICD-10 code description
recurrent fever

Primary outcomes

1

Description
Evaluation of disease attacks in case and control groups
Timepoint
Monthly
Method of measurement
Clinical examination and completion of checklist

Secondary outcomes

empty

Intervention groups

1

Description
Intervention group: In addition to the previously used treatments, treatment with lactogam (manufactured by Bio Fermentation Company), which contains the probiotic

Streptococcus salivarius K12 (> 10^9CFU), should be used by the patient as a suction for 4 months and at night before going to bed.

Category

Treatment - Drugs

2

Description

Control group: Previous standard treatments will include acetaminophen and the NSAID prednisolone. A placebo will also be used in this group (control) where the placebo will be similar in shape and color to the intervention group. The method of prescribing it will be the same

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

بیمارستان اکبر

Full name of responsible person

Nafiseh Pourbadakhshan

Street address

Namaz Blvd

City

مشهد

Province

Razavi Khorasan

Postal code

9166655688

Phone

+98 51 3859 6431

Email

pourbadakhshann@mums.ac.ir

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Mashhad University of Medical Sciences

Full name of responsible person

Majid Ghayour-Mobarhan

Street address

Namaz Blvd

City

Mashhad

Province

Razavi Khorasan

Postal code

9138813944

Phone

+98 51 3841 1538

Email

vcresraech@mums.ac.ir

Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

Mashhad University of Medical Sciences

Proportion provided by this source

100

Public or private sector

Public

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin

Type of organization providing the funding

Academic

Person responsible for general inquiries

Contact

Name of organization / entity

Mashhad University of Medical Sciences

Full name of responsible person

Nafiseh Pourbadakhshan

Position

Associate professor

Latest degree

Specialist

Other areas of specialty/work

Pediatrics

Street address

17 shahrivar 5

City

Mashhad

Province

Razavi Khorasan

Postal code

9166655688

Phone

+98 51 3859 6431

Email

pourbadakhshann@mums.ac.ir

Person responsible for scientific inquiries

Contact

Name of organization / entity

Mashhad University of Medical Sciences

Full name of responsible person

Nafiseh Pourbadakhshan

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Phone
+98 51 3859 6431
Email
pourbadakhshann@mums.ac.ir

Person responsible for updating data

Contact
Name of organization / entity
Mashhad University of Medical Sciences
Full name of responsible person
Nafiseh Pourbadakhshan
Position
Associate professor
Latest degree
Specialist
Other areas of specialty/work
Pediatrics
Street address
17 shahrivar5
City
Mashhad
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Postal code
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Email
pourbadakhshann@mums.ac.ir

Sharing plan

Deidentified Individual Participant Data Set (IPD)
Undecided - It is not yet known if there will be a plan to make this available
Study Protocol
Undecided - It is not yet known if there will be a plan to make this available
Statistical Analysis Plan
Undecided - It is not yet known if there will be a plan to make this available
Informed Consent Form
Undecided - It is not yet known if there will be a plan to make this available
Clinical Study Report
Undecided - It is not yet known if there will be a plan to make this available
Analytic Code
Undecided - It is not yet known if there will be a plan to make this available
Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available