

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

09 Jun 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 receives lactogam and the other group gets placebo.

##### 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 Criteria 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<sup>9</sup>CFU), 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**

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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**

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**Postal code**

9138813944

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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

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17 shahrivar 5

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Mashhad University of Medical Sciences

**Full name of responsible person**

Nafiseh Pourbadakhshan

**Position**

Associate professor

**Latest degree**

Specialist

**Other areas of specialty/work**

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**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

**Province**

Razavi Khorasan

**Postal code****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