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Food Allergy treatment with Butyrate (FAB)

Submission date 11/01/2021	**Recruitment status** Stopped	[X] Prospectively registered [ ] Protocol
Registration date 22/02/2021	**Overall study status** Stopped	[ ] Statistical analysis plan [ ] Results
Last Edited 25/10/2024	**Condition category** Other	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The prevalence of allergic diseases and asthma are increasing worldwide; they doubled in the last 20 years. Food allergy has recently started to increase too. In westernized countries, around 1 in 20 children is allergic to at least one food. Food allergy can cause life-threatening anaphylactic reactions. Moreover, several studies have shown that food allergy has a strong negative impact on the quality of life.

Nutrition is a crucial environmental factor in early life, influencing the development of the child's microbiota and immune system. It has been shown that consumption of cow's milk products, such as yogurt and butter, might have preventive effects on the development of allergic diseases, such as food allergy. Yogurt and other milk products constitute favorable growth conditions for the gut microbiota. Furthermore, they contain high levels of the immunomodulatory molecules short-chain fatty acids (SCFAs), which are associated with protection against allergic diseases in children.

With the rising prevalence of food allergy, a potentially life-threatening disease, and its major impact on the quality of life, treatments for food allergy are needed.

The study aims to increase tolerance to food proteins using a strategy based on the consumption of a diet rich in butyrate. Butyrate is a dietary component commonly found in cow's milk fat, such as cheese and butter. Increasing the threshold dose of butyrate could help to further develop protocols of food oral immunotherapy for patients (children) with food allergies.

Who can participate?
Children aged between 4 and 13 with food allergies. Recruitment will be from the Children's Hospital of Eastern Switzerland in St. Gallen, University Children's Hospital of Bern, and Hochgebirgsklinik (HGK) Davos.

What does the study involve?
The participants in the study will be randomly divided into two groups. One group will follow a diet with the addition of cow's milk products into their normal diet. Only milk products that are available in Switzerland will be included in the diet. The amount of cow's milk products

introduced is related to a certain amount of butyrate, that the milk products contain. These additional cow's milk products will be included in the diet of children for 5 weeks. This will be compared to the second group of children continuing their normal diet.

What are the possible benefits and risks of participating?
The participants have no clear direct benefits as a result of participating in the study. However, the results of the study might support the development of diet patterns that might reduce the symptoms of food allergic children.

Adverse events (AE) related to the study-specific diet will be reported in a daily diary by the participants during the study.

Where is the study run from?
The Children's Hospital of Eastern Switzerland in St. Gallen (Switzerland)

When is the study starting and how long is it expected to run for?
From March 2020 to April 2024

Who is funding the study?
The Kühne Foundation (Switzerland) and the Ulrich Müller Allergy Foundation (Switzerland)

Who is the main contact?
Ms Caroline Roduit, caroline.roduit@kispi.uzh.ch

Contact information

Type(s)
Scientific

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Additional identifiers

Study information

Scientific Title

Monocentric, randomised single-blind, placebo-controlled clinical study to assess whether a Multicentric, randomised clinical pilot-study to assess whether a diet rich in milk products could increase oral tolerance to the incriminated food protein in food allergy children

Acronym
FAB

Study objectives
A diet rich in butyrate will help to improve the oral tolerance to the incriminated food protein among children with food allergies.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/12/2020, Ethikkommission Ostschweiz (Scheibenackerstrasse 4, 9000 St.Gallen, Switzerland; +41 58 411 2891; sekretariat@ekos.ch), ref: 2020-02045

Primary study design
Interventional

Study design
Monocentric single-blind randomized placebo-controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Food allergy among children

Interventions
Children with food allergy confirmed by an oral food challenge will be randomly allocated to either:
1. Intervention group, where participants will receive cow's milk products daily corresponding to a minimal daily total butyrate intake of 1.5 g for children aged 4 to 8 years, and 2 g for children aged 9 to 13 years
2. Control group, where participants will continue a normal diet low in cow's milk products (corresponding to a daily butyrate level lower than 0.75 g for children aged 4 to 8 years, and lower than 1 g for children aged 9 to 13 years)

An electronic list of dairy products high in butyrate will be provided by a dietician. CHildren will follow the diet for 5 weeks.

The randomization will be done with a 1:1 ratio. The allocation will be stratified for the study sites and the two age/dosage groups (4 to <9 years, and 9 to 13 years), such that the two treatment arms are balanced with respect to the age/dosage groups. The trial statistician is responsible to create a corresponding randomization list and is responsible that the randomization list is available in concealed from, i.e. in sealed envelopes for each individual patient, to the study team at each site.

Intervention Type
Supplement

Primary outcome(s)
1. Minimum amount of food protein needed to provoke an allergic reaction, defined as achieving an increase of 1 dose-level of the LOAEL (lowest observable adverse event level), measured using a standard oral food challenge (OFC) with the food allergen, at baseline and 5 weeks. The OFC will be done with the incriminated food, following a standard procedure with 7 dose-levels of food protein (3 mg, 10 mg, 30 mg, 100 mg, 300 mg, 1000 mg, and 3000 mg) at an interval of at least 20 min.

Key secondary outcome(s)
1. Frequency of gastrointestinal side effects measured using the change of short-chain fatty acid (SCFA) level in fecal samples using ultra-high performance liquid chromatography (UHPLC) from baseline to 18 days, and 28 to 42 days
2. Immune parameter levels measured using blood samples (sIgE, T cells population) from baseline to between 28 and 42 days

Completion date
30/04/2024

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Aged 4-13 years
2. Food allergy (defined as a positive food challenge and positive sensitization to the same food allergen)
3. Staying at the rehabilitation clinic Hochgebirgsklinik (HGK), in Davos, for ≥6 weeks, seen by local pediatric physicians in Davos or Klosters, or recruited in the pediatric outpatient clinics of the University Children’s Hospital of Bern or the Children’s Hospital of Eastern Switzerland in St. Gallen

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
4 Years

Upper age limit
13 Years

Sex
All

Key exclusion criteria
1. History of severe anaphylaxis defined by significant hypotension
2. Milk allergy (as the intervention will be based on a diet with dairy products)
3. Severe and uncontrolled asthma
4. Severe cardiac diseases
5. Treatment with beta-blockers
6. Pre-existing doctor diagnosis of immunodeficiencies
7. Children that already at the beginning of the study consume a high amount of cow's milk products (corresponding to a butyrate level lower than 0.75 g for children aged 4-8, and lower than 1g for children aged 9-13)

Date of first enrolment
01/03/2021

Date of final enrolment
28/02/2024

Locations

Countries of recruitment
Switzerland

Study participating centre
Hochgebirgsklinik (HGK)
Herman Burchard Str. 1
Davos
Switzerland
7265

Sponsor information

Organisation
Christine Kühne – Center for Allergy Research and Education (CK-CARE)

Funder(s)

Funder type
Research organisation

Funder Name
Christine Kühne – Center for Allergy Research and Education

Alternative Name(s)
CK-CARE

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Caroline.Roduit@kispi.uzh.ch.
All of the individual participant data collected during the trial, after identification will be available immediately following peer-reviewed publication with no end date. There will be no access criteria data and data will be shared with anyone who wishes to access the data. Other available documents include the Study Protocol, Statistical Analysis Plan, Informed Consent Form, Clinical Study Report, Analytic Code, and ethical or legal restrictions.

IPD sharing plan summary
Available on request