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The effectiveness and safety of fucoidan for atopic dermatitis

Submission date
05/02/2023

Recruitment status
No longer recruiting

Registration date
16/02/2023

Overall study status
Completed

Last Edited
14/02/2023

Condition category
Skin and Connective Tissue Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Atopic dermatitis (AD), a chronic-recurrent inflammatory skin disorder, is one of the most common skin diseases, characterized by skin hypersensitivity, intense itching, and eczema skin lesions. The prevalence of atopic dermatitis in Taiwan is 6.7%. The clinical manifestations include erythematous patches with exudation, blistering and crusting at early stages and scaling, fissuring (cracking) and lichenification (thickening) at later stages. AD can manifest at any point in life, but most often develops during childhood. Patients with AD are at risk for the development of allergic disorders, such as allergic rhinitis and asthma. AD can affect health-related quality of life. That is, the higher the AD severity, the worse the health-related quality of life. Moreover, AD has a substantial negative impact on work productivity and daily activity. Therefore, more effective AD treatments must be developed to resolve the burden of the disease on patients' quality of life and work productivity.

Fucoidan, a polysaccharide found in brown seaweeds, has been studied for its possible therapeutic potential for the treatment of AD. Previous studies have shown that fucoidan can suppress IgE induction in peripheral blood mononuclear cells derived from AD patients, as well as inhibit mast cell degranulation in vitro and reduce the levels of IL-4 and histamine in vivo. In addition, it has been shown to effectively improve wound healing, reduce infiltration of eosinophils, and decrease the expression levels of AD-associated cytokines. However, there have not been any clinical studies conducted to test the effectiveness of fucoidan in humans with AD. Due to its anti-inflammatory properties and the promising results of previous in vitro and in vivo studies, this study looks at the use of fucoidan to treat AD.

Who can participate?
Adults with AD

What does the study involve?
The subjects were enrolled by dermatologists and traditional Chinese medicine (TCM) doctors, after considering the inclusion and exclusion criteria. Written informed consent was obtained from all eligible subjects before participation. A total of 91 participants were randomly assigned 2:1 to receive either low-molecular-weight fucoidan or placebo for 12 consecutive weeks. A total of four in-person visits for assessing symptom severity were arranged for each participant with

the following schedule: day 0 (baseline), week 6, week 12 (end of low-molecular-weight fucoidan /placebo), and week 16 (end of the trial). Other outcome assessments were recorded using self-assessed questionnaires at baseline, week 6, and week 12. Blood samplings were done three times (baseline, week 12, and week 16) for AD-related cytokine assessment, IgE, C-reactive protein (CRP), erythrocytes sedimentation rate (ESR), differential blood count, and biochemical profiles of the hepatic and renal function. The results were evaluated in order to realize the effect of low-molecular-weight fucoidan in the treatment of atopic dermatitis.

What are the possible benefits and risks of participating?
The possible benefits are participants may achieve improvements in symptom severity of atopic dermatitis and also show improvements in their levels of IgE, and eosinophils. The possible risk to participation is mild diarrhoea initially, which may decrease in severity over time.

Where is the study run from?
Chang-Gung Memorial Hospital (CGMH) (Taiwan)

When is the study starting and how long is it expected to run for?
March 2017 to July 2021

Who is funding the study?
Hi-Q Marine Biotech International Ltd (Taiwan)

Who is the main contact?
Pin-Han Wang, eevelyn1980@gmail.com (Taiwan)

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
SCRPD1G0241

Study information

Scientific Title
The efficacy and safety of low-molecular-weight fucoidan in patients with atopic dermatitis: A randomized, double-blind, placebo-controlled trial

Study objectives
Low-molecular-weight fucoidan can improve atopic dermatitis

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 06/03/2017, Chang-Gung Medical Foundation Institutional Review Board (No 199, Dunhua N. Rd, Songshan Dist, Taipei City 105406, Taiwan (ROC); +886 3 3196200 ext 3711; ccyi@cgmh.org.tw), ref: 201601520A3C601

Primary study design
Interventional

Study design
Single-centre interventional double-blinded randomized placebo-controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Atopic dermatitis

Interventions
Fucoidans have been reported to have various pharmacological effects, including anti-cancer, anti-virus, anti-inflammatory, immunomodulatory, anti-pathogen adhesion/infection activities, antidiabetic, and reducing the infection of Helicobacter pylori. A previous study has reported that fucoidan can suppress IgE induction in peripheral blood mononuclear cells derived from

patients with atopic dermatitis (AD). One pilot study observed that topical application of fucoidan could mitigate symptoms of AD in the DNCB-induced mice model by suppressing Th2 cell-mediated immune response. In a study including in vitro and in vivo AD models, fucoidan has been shown to effectively inhibit mast cell degranulation and lower the levels of IL-4 and histamine. And, the systemic improvements included suppressing epidermal hyperplasia, improving wound healing, reducing infiltration of eosinophils, and decreasing the expression levels of AD-associated cytokines.

In this study, a diagnosis of AD is made by a dermatologist. The nursing assistants had a background in public health and nursing. After signing the written informed consent, each participant is assigned a project number. A randomization code list is generated by Hi-Q Marine Biotech International Ltd with the proportion 2:1 of the exam group and the placebo group, respectively. And a pharmacist will give blinded capsules according to the project number in order. Participants, pharmacists, outcome assessors, and investigators are blinded to the outcome of randomization. The randomization code list was unblinded after the trial was completed.

Low-molecular-weight capsules fucoidan or placebo capsules are delivered to participants face-to-face individually to be taken at home. The participants are asked to keep a daily diary recording a checklist of capsules taken per day, skin symptoms and signs, and the use of western medicine. Participants in the study group orally ingest low-molecular-weight fucoidan capsules 2 times a day before meals for 12 weeks, while those in the control group are given a placebo capsule. The following dosing is used: in patients whose body weight is over 40 kg dosing is 4.0g /day (4 capsules twice daily); between 20 kg to 40 kg is 3.0g/day (3 capsules twice daily); below 20 kg is 2.0g/day (2 capsules twice daily); and, below 10 kg is 1.0g/day (1 capsule twice daily).

The primary outcome measures in this study are symptom severity of AD assessed using the SCORAD Index. The outcome assessors are Traditional Chinese medicine(TCM) doctors which were taught SCORAD by the dermatologists and all made a consensus on the evaluation of SCORAD. The extent and intensity of AD lesions are scored as objective indicators and pruritus and sleeplessness as subjective indicators.

The secondary outcomes were the quality of life, the sleep quality, and the parameters related to the immune system, including IgE, WBC, eosinophil, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), interleukin (IL)-4, IL-12, IL-13, interferon-γ (IFN-γ), and the percentage of CD4+ and CD8+ T cells. Quality of life was assessed using the validated Chinese version of Dermatology Life Quality Index (DLQI) questionnaire for patients over 16 years old, as the Children’s Dermatology Life Quality Index (CDLQI) questionnaire was used for patients under the age of 16. Sleep quality was evaluated using the validated Athens Insomnia Scale (AIS) in Chinese version (CAIS-8) (CAIS-8 was validated in adults).

Intervention Type
Supplement

Primary outcome(s)
Symptom severity of atopic dermatitis measured using the Severity Scoring of Atopic Dermatitis (SCORAD) index on day 0 (baseline), week 6, week 12 (end of low-molecular-weight fucoidan /placebo), and week 16 (end of the trial)

Key secondary outcome(s)

The following questionnaires were completed at baseline, week 6, week 12 and week 16:
1. Quality of life measured using the validated Chinese version of the Dermatology Life Quality Index (DLQI) questionnaire for patients over 16 years old, and the Children's Dermatology Life Quality Index (CDLQI) questionnaire for patients under the age of 16 years old
2. Sleep quality measured using the validated Athens Insomnia Scale (AIS) Chinese version (CAIS-8)

The following parameters related to the immune system were measured in blood samples at baseline, week 12, and week 16:
3. Parameters related to the immune system, including IgE, white blood cells, eosinophil, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), interleukin (IL)-4, IL-12, IL-13, interferon-γ (IFN-γ), and the percentage of CD4+ and CD8+ T cells. Blood samples from participants were sent to the department of Laboratory Medicine in Taoyuan Chang Gung Memorial Hospital for testing of IgE, WBC, eosinophil, ESR, CRP, AST, and ALT. For examination of lymphocyte subsets, samples were labeled with antibodies against CD4 and CD8 (BD Biosciences, San Jose, USA). The samples were analyzed by flow cytometry using appropriate isotype controls. Cytometry analyses were performed using BD FACSCanto™ II Clinical Flow Cytometry System equipped with FASDiva Software (BD Biosciences). Serum cytokines levels (IL-4, IL-12, IL-13, Interferon-γ), were measured by an enzyme-linked immunosorbent assay (ELISA) using commercially available kits according to the manufacturer's instructions (Quantikine, R&D System, Minneapolis MN, USA).

4. The average frequency of using western medicine (steroid ointment or oral antihistamine) measured using patient-reported diaries on the days/week during baseline, weeks 1-6, weeks 7-12, and weeks 13-16

Completion date
31/07/2021

Eligibility

Key inclusion criteria
1. Male and female patients between 4 and 60 years of age
2. Evidence of itchy skin (or parental report of scratching or rubbing), combined with three or more of the following:
2.1. History of involvement of the skin creases (e.g., fronts of the elbow, backs of knees, fronts of ankles, and areas around the neck or eyes)
2.2. History of asthma or hay fever
2.3. History of generally dry skin in the past year
2.4. Onset in a child under two years of age
2.5. Visible flexural dermatitis
3. SCORing Atopic Dermatitis (SCORAD) score greater than or equal to 16 points
4. Those who voluntarily agree to participate and sign the informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Mixed

Sex
All

Total final enrolment
91

Key exclusion criteria
1. Other eczema disorders, such as contact dermatitis or seborrheic dermatitis, etc., assessed by a dermatologist
2. Other dermatological diseases related to skin pruritus, assessed by a dermatologist
3. Oral/injected steroids, leukotriene antagonists, immunosuppressants, systemic photochemotherapy, immunotherapy, allergen-specific immunotherapy, or Chinese herbal medicine within 1 month before enrollment
4. Unable to take the study medicine as scheduled or cooperate in filling out the questionnaire and taking a blood test
5. Allergy to fucoidan
6. Hyperthyroidism history
7. Suffering from serious infection requiring hospitalization(e.g., pneumonia, cellulitis, or sepsis) , assessed by a clinician
8. Severe dysfunctions of the organ (e.g., heart failure, liver failure, liver cirrhosis, or renal failure (eGFR <60 mL/min/1.73 m2)), assessed by a clinician
9. Women in pregnancy or in preparation for pregnancy, and those in lactation

Date of first enrolment
15/12/2017

Date of final enrolment
30/06/2020

Locations

Countries of recruitment
Taiwan

Study participating centre
Chang-Gung Memorial Hospital
No. 5, Fuxing St.
Guishan District
Taoyuan City
Taiwan
333423

Sponsor information

Organisation
Linkou Chang Gung Memorial Hospital

Funder(s)

Funder type
Industry

Funder Name
Hi-Q Marine Biotech International Ltd

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 4	26/04/2018	14/02/2023	No	Yes
Participant information sheet	version 3	26/04/2018	14/02/2023	No	Yes