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Effect of a food supplement on pro-inflammatory and pro-resolving mediators in patients with post-COVID-19 condition

Submission date
14/06/2024

Recruitment status
No longer recruiting

Registration date
25/06/2024

Overall study status
Completed

Last Edited
02/07/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
This study aimed to evaluate the eicosanoid and pro-resolutive parameters in post-COVID Syndrome (PCS) patients during 12 weeks of supplementation with a marine oil enriched in specialized pro-resolving mediators (SPMs).

Who can participate?
Adult patients with a PCS who have had a positive COVID-19 test (PCR, fast antigen test, or serologic test) and persistent symptoms related to COVID-19 at least 12 weeks before their enrolment in the study

What does the study involve?
The study compares three groups with daily intakes of 500, 1500 and 3000 mg of the product against a control group that does not use the product. The study will evaluate several parameters, including polyunsaturated fatty acids (EPA, DHA, ARA, DPA), SPMs (such as 17-HDHA, 18-HEPE, 14-HDHA, resolvins, maresins, protectins, and lipoxins), and eicosanoids (prostaglandins, thromboxanes, and leukotrienes). Clinical symptoms of fatigue and dyspnea will be assessed using questionnaires.

What are the possible benefits and risks of participating?
This supplementation might be beneficial by preventing the cytokine storm observed in severe manifestations of COVID-19 disease, as the SPMs may enforce the pro-resolutive axis of inflammatory processes. This also helps improve chronic courses associated with heart and lung tissue inflammation. Also, supplementation with SPMs or their precursor metabolites may improve pathologic conditions for recovered or vaccinated subjects. The increase in SPMs observed in sera of PCS patients might be effective in managing this chronic situation.

Also, the improvement in fatigue and dyspnoea is promising. The supplementation with this marine oil enriched in SPMs hence represents an approach to managing PCS patients.

Risks are potential allergies against fish oil.

Where is the study run from?
Insud Pharma (Spain)

When is the study starting and how long is it expected to run for?
January 2022 to December 2023

Who is funding the study?
Insud Pharma (Spain)

Who is the main contact?
PhD MD Pedro Antonio Regidor, pedro-antonio.regidor@exeltis.com

Contact information

Type(s)
Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Pro-resolving inflammatory effects of a marine oil enriched in SPMs supplement and its implication in patients with a post-COVID syndrome

Acronym
Chesolvov-19

Study objectives
Considering the available data, the use of food supplements rich in Omega-3 fatty acids will not be related to the onset of adverse reactions, and the expected rise of specialized pro-resolving mediators (SPMs) will be associated with a clinical improvement in the symptoms of patients with post-COVID syndrome (PCS), which, in turn, could endorse the use of the supplement as an addition for the management of the disease.
The measurement of the plasma and serum concentrations of pro-inflammatory (prostaglandins and leukotrienes) and pro-resolving lipid mediators (lipoxins, resolvins, protectins, maresins, and monohydroxylated mediators derived from EPA and DHA) in patients with PCS, provided precious information about the immunological response of the patients regarding the inflammatory condition caused by the infection.
The study aims to describe the immunological capacity and inflammatory response of this supplement on PCS patients on the lipidome level and on the clinical entities dyspnea and fatigue compared to healthy individuals by establishing profiles of the LM and their precursor molecules in plasma and serum of the test groups and analyzing the clinical devolvement of the patients.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 23/03/2021, Comité de Ética de la Investigación Santiago-Lugo (Avda. Fernando de Casas Novoa, nº 37, Portal A-B, 1º planta, Santiago de Compostela, 15707, Spain; +34 981 555 103; acis@sergas.es), ref: 2012/097

Study design
Randomized placebo-controlled double-blind parallel-group trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Medical and other records

Study type(s)
Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Post-COVID syndrome

Interventions
This study tests treatment with Omega 3 fatty acid lipid mediators. It is designed as a randomized, double-blind, placebo-controlled trial, with four parallel supplement groups to assess the efficacy of a food supplement enriched in specialized pro-resolving mediators (SPMs) in patients with post-COVID syndrome (PCS). The measurements included pro-inflammatory and pro-resolution lipid mediator levels and perceived fatigue and dyspnoea measured through subjective questionnaires. The safety and tolerability of the investigational product (IP) will also be evaluated.

The study will be planned as a proof of concept; it is a pilot study that aims to determine the effect of increasing food supplement doses. Three different amounts of the supplement (daily use of 500, 1500 and 3000 mg) will be tested and controlled with a placebo. An additional low-dose group has been added, independent of the other two, that is not regulated with the same objectives, to test the supplement's effect on the levels of pro-inflammatory and pro-resolving lipid mediators.

Patients who fulfil all the inclusion criteria (and none of the exclusion criteria) who are willing to participate will sign an informed consent (IC) form and will be randomized to one of the four treatment options, three of which correspond to the double-blind placebo-controlled trial (A, B, C), and the fourth independent, non-controlled, low dose group (X).

No follow-up phase is planned after the study.

Measurement of outcome variables:
In this study, the lipid mediator laboratory analyses will be conducted at Solutex GC SL (for methodology see ref (PMID: 38003333). In brief, the extraction of lipid mediators from plasma and serum samples involved a solid phase extraction (SPE) process. Plasma or serum samples will be mixed with internally deuterium-labeled standard solutions at 500pg, enabling quantification of analytes. SPE will be performed using established protocols after protein removal through precipitation and centrifugation. Following elution from the SPE column using organic solvents, extracts will be dried and resuspended before injection into an LC-MS/MS system. The LC-MS/MS system employed a Qtrap 5500 (Sciex) equipped with a Shimadzu LC-20AD HPLC pump. A Kinetex Core-Shell LC-18 column will be used with a binary eluent system.

Intervention Type
Supplement

Primary outcome measure

The following primary outcome measures are assessed using lipid mediator laboratory analyses at baseline, 4 and 12 weeks of use:
1. Blood samples and analytics of Polyunsaturated fatty acids: EPA, DHA, ARA, DPA.
2. Monohydroxylated specialized pro-resolving mediators (SPMs): 17-HDHA, 18-HEPE, 14-HDHA. SPMs: Resolvins (RvE1, RvD1, RvD2, RvD3, RvD4, RvD5), Maresins (MaR1, MaR2), Protectins (PD1, PDX), Lipoxins (LXA4, LXB4.
3. Pro-inflammatory eicosanoid lipid mediators: Prostaglandins (PGE2, PGD2, PGF2α.), Thromboxanes (TxB2), Leukotrienes (LTB4)

Secondary outcome measures
1. Fatigue measured using the Fatigue Severity Scale (FSS) test from at baseline, visit 2 (4th week of treatment, day 28) and to the end of the study (day 84 of treatment)
2. Dyspnea measured using the Modified Medical Research Council (mMRC) Dyspnea Scale at baseline, visit 2 (4th week of treatment, day 28) and to the end of the study (day 84 of treatment)

Overall study start date
01/01/2020

Completion date
31/12/2023

Eligibility

Key inclusion criteria
1. Adult patients with post-COVID-19 conditions, both genders, between 18 and 70 years old
1.1. Patients with clinical criteria that prove the COVID-19 infection: Diagnosis confirmed using test for COVID-19: PCR, Rapid antigen test, serological test). Symptoms must persist longer than the 12 week after the beginning of the symptoms.
2. Patients with fatigue/asthenia, dyspnea and one of the following:
2.1. General malaise
2.2. Headaches
2.3. Low mood
2.4. Muscular pain
3. Body mass index between 18,5 and 30 kg/m2
4. With the ability to provide informed consent
5. Women who participate in the study must comply one of the following conditions:
5.1. Unable to get pregnant: women who had surgical sterilization or over two years after menopause
5.2. Fertile women must have a negative pregnancy test prior their inclusion in the study (conducted during screening) and use a highly efficient contraceptive method, which are: hormonal contraceptives, intrauterine devices, condoms together with spermicide and gel, partner's surgical sterilization (vasectomy) or total sexual abstinence during the study. The use of these contraceptive methods must last, at least 3 months after the last dose of the study products.

Participant type(s)
Patient

Age group

Mixed

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
55

Total final enrolment
53

Key exclusion criteria
To participate in the study, patients must comply with none of the following exclusion criteria:
1. Pregnant or breastfeeding women
2. Unable to use a highly efficient contraceptive method
3. Recruited in another clinical trial
4. Subjects involved in another clinical trial 4 weeks before their inclusion
5. Patients with any concomitant illness or condition that could affect significantly the hematologic, renal, endocrine, pulmonary hepatic, gastrointestinal, cardiovascular, immunologic, central nervous, dermatologic or any other system, with the exceptions stated in the inclusion criteria
6. Use of Immunosuppressant drugs or prolonged or maintained use of anti-inflammatory drugs and/or corticoids
7. Hypersensitivity, allergy or idiosyncratic reaction to omega-3 acids. Fish or soya allergies.

Date of first enrolment
01/01/2022

Date of final enrolment
01/02/2023

Locations

Countries of recruitment
Spain

Study participating centre
Facultad de Medicina, Universidad de Zaragoza
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Sponsor information

Organisation
Insud Pharma

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Insud Pharma

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
01/09/2024

Individual participant data (IPD) sharing plan
The datasets generated during the current study will be available upon request from the principal investigator PhD MD Pedro Antonio Regidor, pedro-antonio.regidor@exeltis.com. Anonymised data will be available in 1-2 weeks. Consent from participants was required and obtained

The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository internally at Insud Pharma (https://www.insudpharma.com/en/) containing all study data.

There are no ethical or legal restrictions or further comments.

IPD sharing plan summary

Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.2	25/05/2021	24/06/2024	No	Yes
Protocol file	version 1.0	26/01/2023	24/06/2024	No	No