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The beneficial effect on short-term fatigue of a food supplement based on pomegranate, vitamin C and vitamins of group B.

Submission date 20/10/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 31/10/2022	**Overall study status** Completed	
Last Edited 02/08/2023	**Condition category** Other	

Plain English summary of protocol

Background and study aims
Growing evidence suggests that vitamins, particularly B vitamins, contribute to the reduction of tiredness and fatigue. The results of some studies identify vitamin deficiency as a potential trigger for short-term fatigue. Therefore, the supplementation of B vitamins and vitamin C could also be useful if tiredness and fatigue are linked to the nutritional deficiency of these substances, due to a reduced dietary intake.
In addition, pomegranate extract and vitamin C are highly effective in counteracting inflammation and oxidative stress, which are often found in subjects suffering from these conditions.

The aim of this study was to evaluate the effectiveness of supplementing the diet with pomegranate extract, vitamin C, and B vitamins, in improving short-term fatigue, and, consequently, the individual's quality of life.

Who can participate?
Healthy subjects, according to the clinical history; aged between 18 and 75 years; who have been in a condition of medium or moderate fatigue and fatigue for at least one month; with FSS score < 5; able to understand and sign the informed consent.

What does the study involve?
The subjects recruited in the present clinical study will consume a food supplement based on a pomegranate extract, vitamin C and B vitamins, or a placebo, for 56 days, based on the randomization group.
Following the above-cited treatment period, participants will undergo a follow-up period of 28 days, in which participants don’t receive any treatments.

What are the possible benefits and risks of participating?
No risks are foreseen. An improvement in the clinical and symptomatological picture of fatigue and quality of life of the subjects randomized in the food supplement group is hypothesized. However, no benefit may be achieved.

Where is the study run from?
Comegen, Naples (Italy)

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

Who is funding the study?
ESSERRE Pharma S.r.l. (Italy)

Who is the main contact?
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Additional identifiers

Protocol serial number
ERIM22_01

Study information

Scientific Title
Study of the efficacy of a food supplement based on pomegranate, vitamin C and B vitamins, in adults with short-term fatigue: monocentric, controlled, randomized, parallel-group, double-blind clinical study.

Acronym
ERIM22

Study objectives
The aim of this study was to evaluate the efficacy of supplementing the diet with pomegranate extract, vitamin C, and B vitamins, in improving short-term fatigue, and, consequently, the individual's quality of life.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/03/2022, Ethics Committee of ASL Napoli1CENTRO (Via Comunale del Principe, 13 /A, 80145, Napoli, Italy; +39 (0)812544495; comitatoetico@aslnapoli1centro.it), ref: Prot n° 94

Primary study design
Interventional

Study design
Interventional monocentric randomized parallel double-blind placebo-controlled clinical trial

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Short-term fatigue

Interventions
The subjects recruited in the present clinical study will consume a food supplement based on a pomegranate extract, vitamin C and B vitamins, or a placebo, for 56 days, based on the randomization group.

Following the above-cited treatment period, participants will undergo a follow-up period of 28 days, in which participants do not receive any treatments.

The randomization sequence will be generated by a statistician using STATA 16 software (Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC) and the randomization list will be kept hidden. The participants will be assigned to each of the two treatment groups (food supplement or placebo) casually and by simple randomization (1:1 allocation ratio). The randomization code will consist of a three-digit number as indicated in the respective Case Report Form (CRF).

In the clinical study, 58 participants will be enrolled and divided into two groups (29 for each group):

- Group 1: food supplement containing pomegranate extract, vitamin C, and B vitamins.
- Group 2: placebo.

Participants will undergo to four visits (baseline = t0; after 28 days of treatment = t1; after 56 days of treatment = t2; after 28 days from the end of treatment = t3) in an outpatient setting. After each clinical visit, all data are filled in the CRF by physicians.
The clinical trial design is reported below:
During the screening visit, subjects will undergo the following investigation to understand if they meet the study participation requirements:
- Administration of the FSS questionnaire.
Subsequently, all enrolled subjects will undergo the following:
- at t0, t1, and t2 (at baseline, 4 weeks, and 8 weeks from the start of treatment) filling in the FSS and SF-12 questionnaires, administered by the investigating physician.
- at t0 and t2 (baseline and 8 weeks from the start of treatment) a peripheral blood sample will be performed for the analysis of the biomarkers described as secondary endpoints.

To evaluate the possible carry-over effect of the food supplement, it was decided to insert a follow-up period, equal to 4 weeks, in which the subjects will not take any treatment and at the end of which it will be administered again FSS (primary outcome) and SF-12 (secondary outcome) questionnaires.

Intervention Type
Supplement

Primary outcome(s)
Fatigue measured by the Fatigue Severity Scale (FSS). Nine-item self-assessment questionnaire that assesses both physical and mental symptoms of fatigue. The subject is invited to read the sentences carefully and, for each of them, must choose a number from 1 to 7 (1 indicates absolute disagreement with the statement, while 7 indicates complete agreement). The answers to the questions must refer to the last two weeks.
TIME FRAME of the assessment: at baseline (t0), 28 days (t1), 56 days (t2) of treatment, and after 28 days from the end of treatment (t3).

Key secondary outcome(s)
1. Measurement of biomarkers related to fatigue and stress conditions. The following biomarkers will be analyzed in blood samples:
1.1. C-reactive protein (CRP)
1.2. Cortisol
1.3. Pro-inflammatory interleukin: IL-6
In addition, the following biochemical parameters will be analyzed in order to evaluate the effect of dietary supplementation with the food supplement:
1.4 Magnesium, Potassium, Calcium,
1.5. Creatine phosphokinase,
1.6. Vitamins of group B,
1.7. Vitamin D.
TIME FRAME of the assessment: at baseline (t0), and at 56 days (t2) of treatment.
2. Measurement of perceived quality of life with the “Short Form Health Survey-12” (SF-12) questionnaire.
TIME FRAME of the assessment: at baseline (t0), 28 days (t1), 56 days (t2) of treatment, and after 28 days from the end of treatment (t3).

Completion date
15/04/2023

Eligibility

Key inclusion criteria
1. Healthy subjects, according to what was determined by the clinical history and by the information provided during the recruitment;
2. Aged between 18 and 75 years;
3. Who has been in a condition of medium or moderate fatigue and fatigue for at least one month;
4. With FSS score < 5;
5. Able to understand and sign the informed consent.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
75 Years

Sex
All

Total final enrolment
58

Key exclusion criteria
1. Have been in fatigue for more than six months;
2. With an FSS questionnaire score> 5;
3. In conditions of pregnancy or breastfeeding;
4. Cognitive disorders that can hinder the response to questionnaires;
5. History of allergy to the ingredients contained in the treatments under study (dietary supplement and placebo);
6. Chronic pathologies or comorbidities from which the condition of fatigue could derive;
7. Malabsorption;
8. History of drug, drug or alcohol addiction or abuse;
9. Eating disorders;
10. Heart disease;
11. Chronic biliary and pancreatic liver diseases;
12. Neoplastic pathologies;
13. Genetic-metabolic diseases;

14. Diabetes;
15. Rheumatological diseases;
16. Chronic hematological diseases.

Date of first enrolment
17/11/2022

Date of final enrolment
02/12/2022

Locations

Countries of recruitment
Italy

Study participating centre
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Sponsor information

Organisation
ESSERRE Pharma S.r.l.

Funder(s)

Funder type
Industry

Funder Name
ESSERRE Pharma S.r.l.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analyzed during the current study will be published as a supplement to the publication of the subsequent results.

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		26/06/2023	02/08/2023	Yes	No