ISRCTN24645566 https://doi.org/10.1186/ISRCTN24645566

Biological, psychological and social markers of fibromyalgia syndrome

Submission date	Recruitment status	[_] Prospectively registered
31/10/2018	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
10/12/2018	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
10/01/2024	Signs and Symptoms	

Plain English summary of protocol

Background and study aims

Fibromyalgia (FM) is a disabling chronic pain syndrome, affecting almost 14 million people In Europe, especially women. In addition to chronic pain, FM is characterized by sleep disturbance, chronic fatigue, irritable bowel symptoms, stiffness, sicca symptoms, tension headaches, interstitial cystitis, dysmenorrhea, skin and gastrointestinal problems. FM has psychological implications, leading to stress-related symptoms, anxiety and depression. Sometimes, psychological and psychiatric problems can occur before and or right after the development of FM, or develop together with it. At the same time, it has been shown that FM presents on an social basis, with social and personal factors, forced identity redefinition, social suffering, lack of agency, lived trauma and subordination status can be considered as FM determinants. Although a combination of social, biological and environmental factors seem to be involved in FM, the development of the disease is not clear yet.

Opioid receptors are part of cells that are one of the main elements in the development of pain. Considering FM is a chronic pain syndrome, we postulate a link between FM and opioid receptors. This study aims to determine whether opioid receptors should be considered as markers of FM.

As psychological and social factors are also involved in FM, this study also aims to identify profiles of FM patients based on these factors.

Who can participate?

Adults with fibromyalgia can participate with in this study. Adults with other chronic musculoskeletal disorders will also be recruited as a positive control group.

What does the study involve?

All participants will have blood samples taken, which will then be analysed for opioid receptors. Participants will also complete psychological questionnaires and an anthropological interview.

What are the possible benefits and risks of participating?

Participants with FM may benefit from participating as the results could help them to receive a precise diagnosis, tailored therapy and a rehabilitation plan. There are no known risks to participants taking part in this study.

Where is the study run from?
Internal Medicine and Rheumatology Department of Sapienza University of Rome (Italy)

When is the study starting and how long is it expected to run for?
March 2018 to March 2020

Who is funding the study?
ISAL Foundation (Italy)

Who is the main contact?
Professor William Raffaeli
wraffaeli@yahoo.it

Contact information

Type(s)
Scientific

Contact name
Prof William Raffaeli

ORCID ID
http://orcid.org/0000-0003-0240-8993

Contact details
Via San Salvador 204
Torre Pedrera
Italy
47922
0541 725166
wraffaeli@yahoo.it

Type(s)
Scientific

Contact name
Dr Valentina Malafoglia

ORCID ID
http://orcid.org/0000-0002-1533-704X

Contact details
Via San Salvador 204
Torre Pedrera
Italy
47922
0541 725166
valentinamalafoglia@yahoo.it

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
4937

Study information

Scientific Title
Lymphocyte μ opioid receptors as an innovative biomarker for fibromyalgia: a biological, psychological and social study for fibromyalgia diagnosis, therapy and rehabilitation

Acronym
FMBPSM

Study objectives
Here we propose a method to define a new fibromyalgia diagnostic strategy, by proposing μ opioid receptor modulation as a marker of FM. Biological data will be correlated to psychological and anthropological analysis, in order to also define new guideline for therapy and rehabilitation. Psychological and anthropological profiles will help to decide the right strategy, leading to a personal and social improvement.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Sapienza University Ethics Committee, 08/03/2018, reference 4937

Study design
Observational prospective multi-centre single-blinded case-control study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Other

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Fibromyalgia

Interventions
All participants with fibromyalgia (FM) will undergo a clinical examination, with a tender points (TP) count and blood sampling.
Blood sample (20ml) will be taken from both FM patients and the control group for molecular analysis. Blood samples will be stored at room temperature for a maximum of 24 hours. Using the blood sample, the expression and function of the μ opioid receptor on the surface of the lymphocytes will be analysed. Cellular and molecular methods and techniques will be applied in order to find specific biological information for each patient. First of all, blood samples will be processed to separate lymphocytes and monocytes. Monocytes will be isolated using a Ficoll density centrifugation gradient and incubated with anti-CD14 antibody conjugated to magnetic beads. Different lymphocyte populations will be obtained after incubation of the CD14 fraction with magnetic beads conjugated with specific antibodies. Purified cells will be used for RNA and protein extraction and analysis. RNA will be obtained using TRIZOL reagent and cDNA will be synthesized by using SuperScriptIII. Real time PCR will be performed following standard protocols, in order to analyze μ opioid receptor mRNA expression. Western blotting analysis will be performed to analyze proteins expression, using μ opioid receptor specific antibody. An aliquot of fresh blood will be used for immunophenotype analysis. Fluorochrome conjugated antibodies, specific for different cell populations, in combination with anti-μ opioid receptor antibodies, will be used to detect the expression of this receptor on white blood cells. Red cells will be removed by FACS Lysing Solution and samples will be analysed using a FACScalibur flow cytometer. In addition, functional analysis of opioid receptors will be performed by testing for cytokines released by lymphocytes and monocytes, in the presence of specific μ opioid receptor agonists and antagonists. The supernatants of stimulated cells will be analyzed using ELISA. All obtained data will be collected in a standardised, computerised, and electronically-filled form for statistical evaluation.
All participants will also complete the following forms (validated Italian versions) for psychological analysis:
1. Fibromyalgia Impact Questionnaire (FIQ)
2. Fibromyalgia Assessment Status (FAS)
3. Health Assessment Questionnaire (HAQ)
4. Illness Perception Questionnaire-Revised (IPQ-R)
5. Coping Strategies Questionnaire-Revised (CSQ)
6. Depression Anxiety and Stress Scale–21 (DASS-21)
7. Chronic Pain Acceptance Questionnaire (CPAQ)
8. Hypochondriasis (Hs) and Hysteria (Hy) scales of the Minnesota Multiphasic Personality Inventory-2 (MMPI-2)
For anthropological analysis, ethnographic interviews will be undertaken by all participants to define specific anthropological assets and explanation models. The McGill Illness Narrative Interview (MINI) will be used, a semi-structured qualitative interview grid designed to elicit illness narratives in health research to better understand health behaviour in socio-cultural context. The interviews will be recorded, with the participants consent, and then completely transcribed for data analysis.

Intervention Type
Mixed

Primary outcome measure

The following are assessed at the first clinical visit (between 0-12 months):
1. Gene expression analysis of the μ opioid receptor, assessed using real-time PCR using blood samples
2. Protein expression analysis of the μ opioid receptor, assessed using Western blotting using blood samples
3. Immunophenotype of the μ opioid receptor, assessed using blood samples
4. Functional receptor analysis, assessed using ELISA using blood samples

Secondary outcome measures
Psychological endpoints
The following are assessed at the first clinical visit (0-12 months):
1. Fibromyalgia status, progress and outcomes, assessed using the Fibromyalgia Impact Questionnaire (FIQ)
2. Fatigue, sleep disturbances and pain, assessed using the FIbromyalgia Assessment Status (FAS)
3. Health status, assessed using the Health Assessment Questionnaire (HAQ)
4. Perceptions of illness, assessed using the Illness Perception Questionnaire-Revised (IPQ-R)
5. Coping strategies, assessed using the Coping Strategies Questionnaire-Revised (CSQ)
6. Depression, anxiety and stress, assessed using the Depression Anxiety and Stress Scale 21 (DASS-21)
7. Acceptance of pain, assessed using the Chronic Pain Acceptance Questionnaire (CPAQ)
8. Hypochondriasis and hysteria, assessed using the Hypochondriasis (Hs) and Hysteria (Hy) scales of the Minnesota Multiphasic Personality Inventory 2 (MMPI-2) respectively

Anthropological endpoints
Analysis of individual elaboration process of pain and disease, in order to identify the elements that occur more frequently in the illness narratives, will be assessed using the McGill Illness Narrative Interview (MINI). These interviews will be conducted during 3-18 months of the study.

Overall study start date
01/01/2018

Completion date
08/03/2020

Eligibility

Key inclusion criteria
1. Diagnosed with fibromyalgia, according to both 1990 and 2010 ACR criteria
2. Aged 18-65 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit

65 Years

Sex
Both

Target number of participants
Seventy adult patients affected by Fibromyalgia; Seventy patients affected by other chronic musculoskeletal disorders (control group).

Key exclusion criteria
Patients who are treated with opioids

Date of first enrolment
08/03/2018

Date of final enrolment
08/03/2019

Locations

Countries of recruitment
Italy

Study participating centre
Fondazione ISAL
Via San Salvador 204
Torre Pedrera
Italy
47922

Study participating centre
IRCCS san Raffaele pisana
Via di Val Cannuta 247
Roma
Italy
00166

Study participating centre
Internal medicine and rheumatology department, Sapienza - University of Rome, Policlinico Umberto I
Viale dell'università 155
Roma
Italy
00161

Sponsor information

Organisation
Nando and Elsa Peretti Foundation International

Sponsor details
Corso Italia 19
Roma
Italy
00198
+39068419906
Info@nandoperettifound.org

Sponsor type
Other

Website
https://www.nandoandelsaperettifoundation.org

ROR
https://ror.org/04kxhtm13

Funder(s)

Funder type
Other

Funder Name
ISAL Foundation

Results and Publications

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

Intention to publish date
08/03/2020

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?
Results article	results	22/02/2020	03/04/2020	Yes	No
Results article	Qualitative results	17/03/2023	10/01/2024	Yes	No