A study focused at identifying disrupted biological factors and patient-tailored interventions for adolescents with Q-Fever Fatigue Syndrome

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON55036

Source
ToetsingOnline

Brief title
Fatigue study in QFS, CFS and childhood arthritis

Condition

- Autoimmune disorders
- Ancillary infectious topics
- Changes in physical activity

Synonym
Chronic Fatigue Syndrome, Q-Fever Fatigue Syndrome

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Ecological Momentary Assessment, Fatigue, Q-Fever, Smartphone application

Outcome measures

Primary outcome

Objective 1: Biological parameters (e.g. immunological profile, HPA axis,

mitochondrial dysfunctioning, gut microbiome)

Objective 2: Fatigue severity based on the weekly outcome measurements on the

smartphone is the primary outcome.

Objective 3: Fatigue severity based on the weekly outcome measurements on the

smartphone.

Objective 4: Fatigue and all (personalized) fatigue associated factors assessed

in the personalized EMA questionnaires.

Objective 5: Fatigue severity based on the weekly outcome measurements on the

smartphone and change in the biological profile at interval T0, T2, T4.

Secondary outcome

Objective 1: none.

Objective 2: quality of life and self-efficacy based on questionnaires at T0-T4.

Objective 3: quality of life and self-efficacy based on VAS-items of weekly

smartphone measurement.

Objective 4: none.

Objective 5: none.

Study description

Background summary

Severe debilitating fatigue is the dominant symptom of Q-fever fatigue syndrome (QFS). However, little research on QFS has been done in adolescents on pathogenesis or therapy. QFS bears resemblance to the fatigue observed in chronic disorders such as Juvenile Idiopathic Arthritis (JIA) and Chronic Fatigue Syndrome (CFS/ME). In recent literature, chronic fatigue is regarded as a generic instead of a disease-specific symptom. Fatigue is considered the result of a patient-specific complex interplay of psychosocial, lifestyle and biological factors. This calls for a comparable approach for the various fatigue syndromes. The proposed study integrates biology and a psychosocial approach to create an in-depth understanding of QFS. Its treatment is investigated by combining two interventions aimed at direct benefit for QFS adolescent patients.

Study objective

The first objective is to explore the biological profile (e.g. the immunological profile, hypothalamic- pituitary-adrenal (HPA) axis, mitochondrial dysfunctioning, the gut microbiome) of adolescents with QFS and related fatigue disorders (CFS/ME, fatigued JIA patients) at baseline as compared to controls.

The second objective is to evaluate across the three patient groups (QFS, CFS/ME and fatigued JIA patients) the effectiveness of two interventions on fatigue severity (primary outcome), quality of life and self-efficacy (secondary outcomes): (1) patient-tailored PROfeel lifestyle advices, which are partly based on an individual dynamic network of fatigue associated factors that are assessed with the Ecological Momentary Assessments (EMA) methodology, and (2) generic dietary advices based on the Dutch Voedingscentrum. In addition, differences in effectiveness will be explored between the three patient groups.

The third objective is to explore on the individual patient level the effectiveness of the two interventions on fatigue severity (primary outcome) and to explore the effectiveness on quality of life and self-efficacy (secondary outcomes).

The fourth objective is to explore individual effects on pre-post intervention change in the dynamic networks for the patient-tailored PROfeel lifestyle advices-first group.

The fifth objective is to explore the relationship between individual differences in the improvement on fatigue and change in the biological profile in the interval T0, T2, T4 (pre-post interventions).

Study design

Objective 1: case-control comparison design.
Objective 2: randomized controlled trial (RCT) with two intervention arms.
Objective 3: multiple single subject experimental case series design.
Objective 4: multiple single subject pre-post DSEM network-estimates comparison design.
Objective 5: multiple single subject experimental case series design.

Intervention

All recruited patients (subgroups) and control groups start with a baseline assessments (T0):
• The biological material (blood, saliva, faeces) is collected at study start (please see below for more details). Children/ adolescents (12-29 yr) with QFS are compared with a healthy control group of siblings/friends with positive Q-fever serology but without fatigue and with Q-fever serological negative controls.
• Questionnaires (outcome and possible predictors/ mediators, both participants and parents). Patients and parents are invited to fill in digitalized questionnaires. Participants were asked to fill out these questionnaires without assistance from their parent(s) or the researcher.

Only the patient groups :
• Four weeks of intensive EMA at T0 (and T2): All patients will be invited to discuss with the trial coordinator which personal factors may be relevant in relation to the fatigue such as pain, dizziness, sleep, activity, school, work, anger, isolation, fear. This will result in a short list of maximal 12 items classified in symptoms, feelings, behavior, activities, cognitions which will be measured 4-6 times a day during 4 weeks using the EMA technology.
• At T0, T2 and T4 all patients will be asked to fill in the outcome questionnaires and to collect biological samples (for storage in biobank). At T2 all patients will have another 4 weeks of intensive EMA.

• Will be followed during the study with weekly outcome measurements on the smartphone. In case patients self-report sufficient improvement in fatigue and/or show clinical significant improvement after the first intervention, they will be asked to complete the weekly smartphone measurements for 12 more weeks after the first intervention. In case patients self-report and/or show clinical significant improvement after the second intervention, they will be asked to complete the weekly smartphone measurements for 12 more weeks after the second intervention. In case patients do not self-report and/or show clinical significant improvement after the second intervention, they will be offered alternative therapy and will be asked to complete weekly smartphone measurement until T5.
• At T5 there is follow-up measurement.

Study burden and risks

patients:
4 weeks intensive questionnaires (EMA) twice
3 vists a 45-60 min combined with regular visit if possible
2x 12 weeks intervention.

In case patients self-report sufficient improvement in fatigue severity and/or show clinically significant improvement in fatigue severity after the first intervention, they are not obliged to participate in the second intervention. If they choose not to enroll in the second intervention, they will be asked to complete the weekly smartphone questionnaire for only 12 more weeks (i.e. until week 28 of the study). In case patients self-report sufficient improvement and/or show clinical significant improvement in fatigue severity after the second intervention, they are also asked to complete the weekly smartphone questionnaire for 12 more weeks (i.e. until week 44 of the study).

Throughout the study, we aim to combine patients research participation as much as possible with regular visits and care in order to minimize participation burden.

healthy controls:
1 visit to the hospital 45 min.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

For all subjects:
• Age of 12-29 years old
• Able to speak, read, understand and write Dutch

Inclusion criteria for QFS-patients:
• Diagnosed with QFS according to the Dutch Guidelines
• Fatigue lasting for at least 6 months
• Debilitating fatigue which started before the age of 18, with detrimental effects on daily functioning (work and/or private situation)
• Seropositive for C. Burnetii
• No diagnoses of chronic Q-fever, recent diagnostics (<3 months ago) showing a IgG fase 1 titer <1:1024 (or 1:512 in the case of immunocompromised patients or patients with vascular prosthesis or heart defect)
• No somatic of psychiatric comorbidity that can explain fatigue at baseline
• No history of fatigue before infection with C. Burnetii, or fatigue critically increased in severity after infection with C. Burnetii.
• For CBT: Fatigue severity subscale (CIS8) score>39

Inclusion criteria for CFS/ME:
• CFS/ME diagnosis according to the CDC criteria before the age of 18
• No diagnosis of QFS
• Fatigue severity subscale (CIS8) score >39

Inclusion criteria for JIA:
• Diagnosed with JIA, at least 3 months on stable medication and a stable disease activity score (JADAS-criteria)
• No diagnosis of QFS
• Expressing fatigue as a major complaint before the age of 18
• CIS8 score >34 (mean + 1 SD)
• Being fatigued for at least 3 months

Siblings/friends (healthy individuals):
• Not severely fatigued (CIS8 < 40)
• The status of C. Burnetii serology will be assessed after inclusion

Exclusion criteria

• Diagnosis of chronic Q-fever ánd active disease
• Cognitive impairment, estimated IQ<70
• Concomitant diagnoses that may explain the fatigue
• Any current and predominated psychiatric comorbidity with could explain fatigue (i.e. major depression disorder, presence of suicidal risk)
• No smartphone

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	22-10-2020
Enrollment:	140
Type:	Actual

Ethics review

Approved WMO Date:	16-06-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	07-09-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-04-2021
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL72103.041.20