Altered interferon-gamma response in patients with Q-fever fatigue syndrome

Published: 25-07-2016
Last updated: 16-04-2024

This study will investigate the value of C. burnetii-specific whole-blood IFNγ and IL-2 production assays in QFS patients that have either recovered, or are still substantially fatigued. This will show us if these assays can serve as...

Ethical review	Approved WMO
Status	Pending
Health condition type	Ancillary infectious topics
Study type	Observational invasive

Summary

ID

NL-OMON42843

Source
ToetsingOnline

Brief title
QFS - IFNgamma

Condition

- Ancillary infectious topics

Synonym
Q-fever, Q-fever fatigue syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Algemene Interne Geneeskunde
Source(s) of monetary or material Support: Stichting Q-support (verlenen subsidie;is GEEN opdracht)

Intervention

Keyword: IFNgamma, IL-2, Q-fever, Q-fever fatigue syndrome

Outcome measures

Primary outcome

• Cytokine concentrations (IL-2 and IFNγ)

• CIS score, subscale on fatigue

Secondary outcome

- Chemokine levels of CXCL 8/9/10/11

- Q-fever serology , using Immunofluorescence Assay (IFA)

Study description

Background summary

Q Fever Fatigue Syndrome (QFS) is a well documented state of prolonged fatigue, following acute Q fever. Up to 20% of patients that are diagnosed with acute Q fever will develop QFS, leading to a substantial burden for the affected patients. To date, no diagnostic test is available to diagnose QFS directly. The diagnosis is based on clinical criteria. Serology is used to exclude chronic Q fever and to confirm a past Q fever infection, but cannot differentiate between past infection and QFS. Serology can also become negative several years after the infection while the patients are still suffering from QFS. Recently our group developed a C. burnetii-specific whole-blood IFNγ production assay, which is a promising diagnostic tool for C. burnetii infection, with similar performance and practical advantages over serology. In addition, a high IFNγ/IL-2 ratio appeared to be indicative of chronic Q-fever, and may be a useful diagnostic marker for chronic Q-fever and treatment monitoring. Based on these results, our group determined the value of these tests in QFS patients. It appeared that IFNγ production assays were able to differentiate QFS patients from healthy seropositive controls, and IFNγ/IL-2 ratio (adding IL-2 production assays) was able to differentiate QFS patients from chronic Q-fever patients. To further investigate the value of this test, we aim to evaluate C. burnetii-specific whole-blood IFNγ production assays (and C. burnetii-specific whole-blood IL-2 production assays) in QFS patients that previously participated in the Qure study that have either recovered from their complaints, or are still experiencing complaints. This enables us to

investigate the value of IFNγ and IL-2 production as biologic parameters of recovery. Using the subscale fatigue of the Checklist Individual Strength (CIS) to assess at time of diagnosis and after treatment, we can specifically investigate the correlation between level of fatigue, i.e. recovered versus non-recovered, and IFNγ and IL-2 production.

Study objective

This study will investigate the value of C. burnetii-specific whole-blood IFNγ and IL-2 production assays in QFS patients that have either recovered, or are still substantially fatigued. This will show us if these assays can serve as potential biologic parameters in the recovery of QFS, and will help us understand if immunopathologic mechanisms play a role in the complaints that are seen in QFS.

Study design

We will determine the value of C. burnetii-specific whole-blood IFNγ and IL-2 production assays in QFS patients that have either recovered, or are still substantially fatigued. Severe fatigue (and therefore no recovery) is defined as a score >= 35 on the subscale fatigue severity of the CIS. Recovery is defined as a score < 35 on the subscale fatigue severity of the CIS + clinical significant change, compared to baseline score on the subscale fatigue severity of the CIS.
After informed consent is obtained, blood will be drawn in 1 Heparine tube of 5ml and 1 Serum tube of 3ml. Whole blood will be divided over 3 0.5ml tubes, each tube will then be stimulated with either C. burnetii Nine Mile RSA 493 Phase I (CbNM), Phytohaemagglutinin (PHA) as a positive control, or Roswell Park Memorial Institute medium (RPMI) as a negative control. Samples will be incubated for 24 hours at 37 *C, after which supernatants will be collected and stored at -20 *C until analysis. IFNγ and IL-2 production will be measured by means of ELISA (IFN γ: Pelikine compact, Sanquin, Amsterdam, the Netherlands.) and multiplex beads assay (Merck Millipore, Billerica, MA, USA), according to the manufacturer*s instructions. Additionally, levels of CXCL 8/9/10/11 will be measured in unstimulated serum samples by means of multiplex beads assay (Bio-Rad, Haryana, India).

The duration of this study is 1 year. Patients will be recruited among previous participants of the Qure study, performed in the Radboudumc, Nijmegen. In this study, the effect of three different treatment regimes, i.e. cognitive behavioral therapy (CBT), doxycycline and placebo, was determined. We aim to recruit only those who received CBT or a placebo, since tetracyclines have the potential to influence T-cell activation and could therefore interfere with IFNγ and IL-2 production assays. Before and after treatment, patients were asked to fill out the CIS (subscale on fatigue) questionnaire. The outcome of this questionnaire can be used as an indicator of recovery in our study.

However, since the post-treatment results are most likely dated in several cases, patients will be asked to fill out this questionnaire once more, indicating whether or not a change in recovery has occurred. Within the next few months (which is still in the one-year follow-up period of the Qure study), patients will receive notification from the coordinating investigator on the outcome of this study. At that time, we aim to inform patients about our study by sending them additional information in a return envelope, providing the option to recline from being contacted for participation in our study. If no recline has been received after two weeks, patients will be asked by telephone if they are willing to participate in our study.

Study burden and risks

Burden: One time collection of blood (1 Heparine tube of 5ml and 1 Serum tube of 3ml) + filling out CIS questionnaire (subscale on fatigue).

Risk: No risks other than local hematoma and vasovagal collapse are related to venous puncture.

Benefit: There will be no direct benefits for the subjects enrolled in this study.

Contacts

Public
Selecteer

Geert Grooteplein-Zuid 10
Nijmegen 6525 GA
NL
Scientific
Selecteer

Geert Grooteplein-Zuid 10
Nijmegen 6525 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Diagnosis of QFS according to national LCI-guideline Q fever fatigue syndrome (QFS);
• Score >=40 on the subscale fatigue of the Checklist Individual Strength (CIS) at time of diagnosis
• Severe functional impairment on Sickness Impact Profile-8 (SIP-8), defined as a SIP total score >=700 at time of diagnosis;
• Age >=18.

Exclusion criteria

• Use of immunosuppressant drugs in the past 3 months ;
• Pregnancy;
• Use of doxycycline in the past 6 months.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	03-05-2016

Enrollment:	104
Type:	Anticipated

Ethics review

Approved WMO Date:	25-07-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-03-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL57578.091.16