The Qure study: Q-fever fatigue syndrome - response to treatment.

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Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON25227

Bron
Nationaal Trial Register

Verkorte titel
The Qure study

Aandoening

In English: adult patients with Q fever Fatigue Syndrome.

In Dutch: volwassenen met het Q-koortsvermoeidheidssyndroom

Ondersteuning

Primaire sponsor: Radboud University Nijmegen Medical Centre
Overige ondersteuning: ZonMW: The Netherlands Organisation for Health Research and Development

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Fatigue severity measured with the Checklist Individual Strength (CIS).

Toelichting onderzoek

Achtergrond van het onderzoek

Abstract publicatie Qure-studie:

Background. Approximately 20% of patients with acute Q fever will develop chronic fatigue, referred to as Q fever fatigue syndrome (QFS). The objective of this randomized controlled clinical trial was to assess the efficacy of either long-term treatment with doxycycline or cognitive-behavioral therapy (CBT) in reducing fatigue severity in patients with QFS.

Methods. Adult patients were included who met the QFS criteria according to the Dutch guideline: a new onset of severe fatigue lasting ≥6 months with significant disabilities, related to an acute Q fever infection, without other somatic or psychiatric comorbidity explaining the fatigue. Using block randomization, patients were randomized between oral study medication and CBT (2:1) for 24 weeks. Second, a double-blind randomization between doxycycline (200 mg/day, once daily) and placebo was performed in the medication group. Primary outcome was fatigue severity at end of treatment (EOT; week 26), assessed with the Checklist Individual Strength subscale Fatigue Severity.

Results. Of 155 patients randomized, 154 were included in the intention-to-treat analysis (doxycycline, 52; placebo, 52; CBT, 50). At EOT, fatigue severity was similar between doxycycline (40.8 [95% confidence interval {CI}, 37.3–44.3]) and placebo (37.8 [95% CI, 34.3–41.2]; difference, doxycycline vs placebo, −3.0 [97.5% CI, −8.7 to 2.6]; P = .45). Fatigue severity was significantly lower after CBT (31.6 [95% CI, 28.0–35.1]) than after placebo (difference, CBT vs placebo, 6.2 [97.5% CI, .5–11.9]; P = .03).

Conclusions. CBT is effective in reducing fatigue severity in QFS patients. Long-term treatment with doxycycline does not reduce fatigue severity in QFS patients compared to placebo.

Doel van het onderzoek

So far no data on effective treatment for Q fever Fatigue Syndrome (QFS) are availabe. At present, it is unclear whether effective treatment for QFS is possible. The objective of this study is to assess the efficacy of two treatment strategies for fatigue and disabilities in QFS: long term treatment with doxycycline or cognitive behavioral therapy (CBT). These treatment modalities will be compared with placebo.

Onderzoeksopzet

Primary outcome CIS: At baseline, 8 weeks and 24 weeks after start treatment.

Secondary outcomes:

1. SIP score: At baseline and 24 weeks after start treatment;

2. SCL90: At baseline and 24 weeks after start treatment;

3. Coxiella serology and PCR: At baseline and 26 weeks after start treatment.

Onderzoeksproduct en/of interventie

Allocation will be randomized:

1. CBT for 24 weeks (n=60);

2. Long-term antibiotic therapy using doxycycline 200 mg once daily for 24 weeks (n=60);

3. Placebo for 24 weeks (n=60)).

At first, randomization will occur between CBT or medication (ratio 1:2). If patients are randomized to the medication group, a second double-blinded randomization will be done by the study pharmacist (department of Clinical Pharmacy, Radboud University Nijmegen Medical Centre). Obviously, allocation to the CBT intervention cannot be blinded. However, the assessor performing the post-treatment assessment does not know if the patient has been allocated to CBT as patients will be instructed not to give this information. The double-blinded randomization assignment will be known to the study pharmacist only.

In more detail, the intervention groups consist of:

1. Cognitive Behavioral Therapy (CBT): CBT will consist of a protocolized intervention of 12 sessions during a period of 24 weeks. It starts with goal setting and psycho-education on the possible role of cognitions and behavior in maintaining the fatigue. The maintaining factors will subsequently be addressed (regulation of sleep-wake cycle, gradual increasing activity, reformulating fatigue related cognitions);

2. Doxycycline: Antibiotic therapy will consist of doxycycline once daily 200 mg (1 capsule) for 24 weeks. Patients will be monitored 4, 8, 16 and 26 weeks after start for side effects (rash, liver enzymes). Antibiotics will be stopped in case of side effects or pregnancy;

3. Placebo: Patients in the placebo group will receive once daily 1 placebo capsule identical in

appearance to the doxycycline capsules for 24 weeks and have the same visits and monitoring for side effects as the patients randomized to doxycycline.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Males or non-pregnant, non-lactating females who are 18 years or older;

2. Laboratory-proven acute Q fever since the year 2007 and/or positive serology fitting a past infection with Coxiella burnetii;

3. Being severely fatigued, defined by scoring 35 or higher on the subscale fatigue severity of the CIS;

4. Being fatigued for at least 6 months;

5. Disabled because of the fatigue, defined by scoring 450 or higher on the SIP;

6. Subjects must sign a written informed consent form.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Fulfilling criteria for chronic Q fever, namely:

A. IFA IgG fase I ≥ 1024, ≥ 3 months after acute Q fever, and/or;

B. Positive Coxiella burnetii PCR on serum or tissue, 1 month after acute Q fever.

2. Acute Q fever in the setting of a prosthetic cardiac valve or aneurysm surgery or stenting necessitating prophylactic use of doxycycline;

3. Pregnancy or unwillingness to use effective contraceptives during the entire study period;

4. Imminent death;

5. Inability to give informed consent;

6. Allergy or intolerance to doxycycline;

7. Somatic or psychiatric illness that could explain the chronic fatigue;

8. Subjects who are currently enrolled on other investigational drug trials or receiving investigational agents;

9. Receiving antibiotics for more than 4 weeks, potentially active against Coxiella burnetii, for any other reason since Q-fever diagnosis;

10. Subjects who are receiving and cannot discontinue barbiturates, phenytoin, or carbamazepine (these drugs may increase the metabolism of doxycycline and therefore reducing half-life of doxycycline);

11. Moderate or severe liver disease (AF, ALAT, ASAT > 3 times the upper limit of normal);

12. Current engagement in a legal procedure concerning financial benefits (only current involvement interferes with the effectivity of cognitive behavioral therapy. Once the appeal procedure ends, subjects can be included).

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-04-2011
Aantal proefpersonen:	180
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	08-03-2011
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2669

Register	ID
NTR-old	NTR2797
Ander register	ZonMw / EudraCT : 205520003-20110307 / 2011-000643-25;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten

Stephan P. Keijmel, Corine E. Delsing, Gijs Bleijenberg, Jos W. M. van der Meer, Rogier T. Donders, Monique Leclercq, Linda M. Kampschreur, Michel van den Berg, Tom Sprong, Marrigje H. Nabuurs-Franssen, Hans Knoop, Chantal P. Bleeker-Rovers; Effectiveness of Long-term Doxycycline Treatment and Cognitive-Behavioral Therapy on Fatigue Severity in Patients with Q Fever Fatigue Syndrome (Qure Study): A Randomized Controlled Trial. Clin Infect Dis 2017 cix013. doi: 10.1093/cid/cix013