The Role of Conditioning for Pharmacotherapeutic Treatments in Rheumatoid Arthritis.

Published: 26-08-2015
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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON44827

Source
ToetsingOnline

Brief title
Conditioning in Rheumatoid Arthritis.

Condition

- Autoimmune disorders

Synonym
rheumatoid arthritis & inflammatory arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Leiden
Source(s) of monetary or material Support: European Research Council Consolidator Grant

Intervention

Keyword: Conditioning, Immune system, Pharmacotherapeutic effects

Outcome measures

Primary outcome

The primary study parameter is the percentage of patients who achieve a drug-free clinical remission (DAS < 1.6) following the tapering period, 12 months after the start of the treatment.

Secondary outcome

Secundary outcome measures include the percentage of patients achieving a clinical remission, clinician- and patient-assessed clinical functioning (e.g., disease activity), laboratory assessments (e.g., cytokine levels), and self-report outcomes (e.g., side effects) following the experimental period (8 months), the tapering period (12 months), and during the end-of-study visit (16 months). Additionally, the possible influence of psychological and genetic predictors on the susceptibility to conditioning will be explored. Finally, a cost-effectiveness analysis will be performed to investigate the cost-effectiveness of the conditioning procedure compared to standard treatment.

Study description

Background summary

Expectancies about health can induce physiological (autonomic, neuroendocrine, and immune) responses that may directly and positively influence health and treatment outcomes. Expectancies can be influenced by conditioning, which is implicit expectancies based on repeated pairing of two previously unrelated

stimuli, leading the one to elicit a similar response when administered alone. This automatic, i.e. conditioning expectancy learning mechanism has been shown to elicit psychological and physiological effects in both healthy and (less often studied) clinical populations. Potentially, this expectancy learning mechanism could be applied to enhance pharmacotherapeutic treatment effects in patients with chronic diseases, with subsequent improvements in psychological and physiological (e.g., immune) functioning. For instance, medication regimens making use of conditioning via principles of variable reinforcement have shown to lead to similar therapeutic effects as full pharmacological treatment, while significantly reducing adverse side effects. However, this has not yet been investigated in patients with rheumatoid arthritis (RA). The ability to influence pharmacotherapeutic effects by means of conditioning could offer new therapeutic possibilities in the treatment of chronic diseases that require long-term pharmacological treatment, such as inflammatory conditions.

Study objective

This study aims to enhance pharmacotherapeutic effects in patients with recent-onset RA by means of conditioning (via a variable reinforcement schedule).

Study design

A multicenter randomized, clinical trial will be conducted in patients with recent-onset RA, closely following the current pharmacological treatment recommendations.
The study is divided into four periods of four months, with both groups receiving the same cumulative amount of active medication during each period:
1. Month 1-4: After initial screening, patients who are eligible for stable standard pharmacological treatment will start on MTX and prednisone.
2. Month 5-8: Only patients who completed the baseline period without significant protocol violations as assessed by the rheumatologist and achieved clinical remission (based on the rheumatologist's opinion, in principle on the DAS < 1.6) will continue to the second phase of the study and will be randomized to one of two groups. The different groups will follow different treatment schedules:
2.1 Control group: standardized treatment dosage (240 mg MTX in total).
2.2 Conditioning group: variable treatment dosage (240 mg MTX in total).
3. Month 9-12: During the third period, MTX will be tapered and discontinued if patients are still in clinical remission (based in the rheumatologist's opinion, in principle on the DAS < 1.6), with dosages either decreasing linearly (Control group) or variably (Conditioning group).
4. Month 16: End-of-study visit.

Intervention

The intervention consists of pharmacological conditioning (variable treatment dosage).

Study burden and risks

As the study closely follows standard treatment protocol for recent-onset RA, most assessments will be conducted during regular patient visits to the hospital (at initial screening and after each 4-month period), with each appointment lasting approximately half an hour to one hour, thus a total time investment of approximately three hours in 16 months. Blood samples will be collected as part of standard care whenever possible. Additional blood samples will be collected in order to determine cytokine values. Questionnaires that will take approximately one hour to complete (totaling about 10 hours over a period of 16 months), can be filled out at home. The study may lead to enhanced treatment effects in the patients within theConditioning group and may lead to new therapeutic possibilities for patients with RA and other chronic diseases requiring long-term pharmacological treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Adult (minimum age of 18 years), recent-onset RA, fluent in Dutch, able to give informed consent, in clinical remission at month 5 after completing the protocolized pharmacological treatment.

Exclusion criteria

- Pregnancy or wish to become pregnant during the study, or childbearing potential without adequate contraception.
- Concomitant treatment with another experimental drug.
- History or presence of malignancy within the last five years.
- Bone marrow hypoplasia.
- Elevated hepatic enzyme levels (ASAT, ALAT > 3 times normal value).
- Serum creatinine levels > 150 umol/l or estimated creatinine clearance of < 75%.
- Uncontrolled diabetes mellitus (according to the rheumatologist).
- Uncontrolled hypertension or moderate to severe heart failure (NYHA class III/IV).
- Alcohol or drug abuse.
- History of infected joint prosthesis within the previous 3 months.
- Serious infections, such as hepatitis, pneumonia, pyelonephrititis in the previous 3 months.
- Chronic infectious disease such as chronic renal infection, chronic chest infection with bronchiectasis or sinusitis.
- History of opportunistic infections such as herpes zoster within previous 2 months.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-03-2016
Enrollment:	94
Type:	Actual

Ethics review

Approved WMO

Date:	26-08-2015
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	09-12-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	27-01-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	05-10-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	15-11-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	13-03-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	26-04-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	01-12-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 20702
Source: NTR
Title:

In other registers

Register	ID
Other	Nederlands Trial Register 5770
CCMO	NL52376.058.15
OMON	NL-OMON20702