Placebo-controlled trial in subjects at ultra-high risk for psychosis with omega-3 fatty acids in Europe

Published: 14-03-2016
Last updated: 20-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Schizophrenia and other psychotic disorders
Study type	Interventional

Summary

ID

NL-OMON53085

Source
ToetsingOnline

Brief title
PURPOSE

Condition

- Schizophrenia and other psychotic disorders

Synonym
Ultra-high risk for psychosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Stanley Medical Research Institute;United States

Intervention

Keyword: omega-3, psychosis, ultra-high risk

Outcome measures

Primary outcome

Transition to psychosis will be defined using the CAARMS criteria or when a subject exceeds the maximally allowed dose of antipsychotics during the study (i.e. equivalent of a total haloperidol use of 10 mg within two months).

Secondary outcome

Symptomatology will be examined using semi-structured interviews and questionnaires including the CAARMS, Positive and Negative Syndrome Scale (PANSS), Global Assessment of Functioning scale (GAF), Clinical Global Impression Scale (CGI) and Beck*s Depression Inventory (BDI). Cognition will be assessed using a computerised battery of neuropsychological tests that capture key deficits associated with psychosis, such as memory, social perception and reasoning. Blood samples will be drawn to assess levels of bioactive lipids, (epi)genetic markers and immune parameters. Finally, brain structure and function are measured in three MRI sessions, consisting of structural MRI, resting state functional MRI, Diffusion Tensor Imaging (DTI), functional MRI during reward processing and magnetic resonance spectroscopy (MRS).

Study description

Background summary

Psychosis is a chronic and severe mental disorder, usually preceded by a prodromal phase of attenuated psychotic symptoms and decline in function.

Intervention during this prodromal state could prevent transition to psychosis, and is therefore of high significance. A recent randomised controlled trial with individuals at ultra-high risk (UHR) for psychosis showed a significantly lower transition rate to psychosis and reduced psychotic symptoms in those subjects who were treated daily with omega-3 fatty acids compared to placebo. Here we further evaluate the potential of omega-3 fatty acids in the prevention of psychosis.

Study objective

Primary objective of this randomised controlled trial is to compare transition rates to psychosis between individuals who are at UHR for developing psychosis and randomised to treatment with omega-3 fatty acids to those randomised to placebo, as determined through the Comprehensive Assessment of At-Risk Mental State (CAARMS) or when a subject exceeds the maximally allowed dose of antipsychotics during the study (i.e. equivalent of a total haloperidol use of 10 mg within two months). Secondary objectives include a comparison between the two treatment arms with regard to discontinuation rate, tolerability, symptomatology, psychosocial and cognitive function, quality of life, blood levels of bioactive lipids, (epi)genetic markers and immune parameters. Third, the ability of both MRI and blood parameters to serve as potential biomarkers that may predict clinical response of UHR subjects will be elucidated. Finally, both cross-sectional and longitudinal comparisons of study parameters will be conducted between UHR subjects and healthy controls.

Study design

A European, multicentre, randomised, double-blind, placebo-controlled clinical trial.

Intervention

Omega-3 fatty acids versus placebo.

Study burden and risks

This study includes eight site visits. The first two visits occur before treatment initiation, and consist of screening for in- and exclusion criteria, a diagnostic interview, and baseline examination of symptomatology, psychosocial and cognitive function, quality of life and drug use. Four blood samples are drawn to perform standard clinical laboratory tests and to assess levels of bioactive lipids, (epi)genetic markers and immune parameters. Subjects will undergo a baseline MRI session of maximum ninety minutes. Both blood sampling and MRI are safe procedures, and standard procedures will be followed to minimise risks. Subsequent visits take place at 1 month, 3 months, 6 months, 1 year, 1.5 years and 2 years after inclusion in the study. During

these visits, interviews and questionnaires performed at baseline will be repeated. At visits 5 and 8, three blood samples will be drawn to assess levels of bioactive lipids, (epi)genetic markers and immune parameters. Transition to psychosis will be assessed at all time points using the CAARMS criteria. UHR individuals younger than 18 years of age will be included in this study, as attenuated symptoms of psychosis typically emerge in adolescence. However, participation in this randomised controlled trial may be of therapeutic benefit to UHR subjects since treatment with omega-3 fatty acids has been associated with prevention of the transition to psychosis. Omega-3 fatty acids are food supplements with important physical health benefits and are minimally associated with adverse effects.

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)

Inclusion criteria

- 13-20 years old (inclusive)
- Written informed consent of the subject. For individuals below the age of legal capacity the parents / legal representatives need to give consent, and the subject can provide assent (whether the latter is required depends on local laws and regulations).
- UHR diagnosis as made using the Comprehensive Assessment of At-Risk Mental States (CAARMS) (Yung et al., 2005). Subjects have to meet one or more of the following criteria: (a) attenuated psychotic symptoms, (b) brief limited intermittent psychotic symptoms (a history of one or more episodes of frank psychotic symptoms that resolved spontaneously within 1 week in the past year), or (c) either the presence of schizotypal personality disorder or a family history of psychosis in a first-degree relative, all three together with a recent decline in function.

Exclusion criteria

•Any clinically significant medical condition that may influence the results of the trial or affect the ability to take part in a trial.
•Laboratory screening values considered clinically relevant by a medical doctor for transaminases, thyroid hormones or coagulation parameters
•Current or past DSM-IV diagnosis of psychosis, as measured with K-SADS-PL
•Intake of an antipsychotic or mood-stabilising agent in the two weeks prior to study inclusion, except for situations as described in section 5.2 of the protocol
•Intake of an antipsychotic agent equivalent to a total haloperidol use of >50 mg in the six months prior to study inclusion, except for situations as described in section 5.2 of the protocol
•A first-degree relative (i.e. parents, offspring or siblings) participating in this study
•UHR diagnosis on the basis of attenuated psychotic symptoms that are entirely explained by acute intoxication
•Current aggression or dangerous behaviour (PANSS G14 score 5 or above)
•Current suicidality / self-harm (PANSS G6 score 7)
•Current DSM-IV diagnosis of alcohol or substance dependence as measured with K-SADS-PL
•Any current or previous neurological disorder, including epilepsy
•History of head injury resulting in unconsciousness lasting at least 1 hour
•IQ < 70
•More than 4 weeks of regular omega-3 supplementation (>2 daily capsules standard strength providing >600 mg combined EPA/DHA) within the last 6 months.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-09-2016
Enrollment:	70
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Omega-3 fatty acids
Generic name:	Fishoil

Ethics review

Approved WMO Date:	14-03-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	27-07-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO	

Date:	20-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-03-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-11-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-08-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-08-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-09-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-07-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	22-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-08-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-09-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-01-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-02-2022
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
EudraCT	EUCTR2015-003503-39-NL
ClinicalTrials.gov	NCT02597439
CCMO	NL55399.041.15