A multicentre randomized double-blind placebo controlled discontinuation trial of methylphenidate.

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Primary objective: To investigate the effectiveness of ongoing treatment with methylphenidate as prescribed in clinical practice beyond two years in children and adolescents. Secondary objectives:(1) to investigate the effects of discontinuation of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cognitive and attention disorders and disturbances
Study type	Interventional

Summary

ID

NL-OMON41851

Source
ToetsingOnline

Brief title
Methylphenidate discontinuation trial

Condition

- Cognitive and attention disorders and disturbances

Synonym
attention disorder, Attention-Deficit/Hyperactivitiy Disorder

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Discontinuation trial, Long-term effectiveness, Methylphenidate, Randomized controlled trial

Outcome measures

Primary outcome

The primary outcome measure will be the clinician based ADHD DSM-5 rating

scale.

Secondary outcome

Secondary outcome measures:

Rating scales

• The Clinical Global Impression Scale of Improvement (CGI-I).

• The criteria of Oppositional Defiant Disorder (ODD)

• Side effects and withdrawal effects will be evaluated by an adapted version

of the Barkley Side Effect Rating scale (BSERS).

• The Sleep Disturbances Scale for Children (SDSC)

• The appetite of the child

• The Retrospective Overt Aggression Scale (R-MOAS)

• The Kindl-R (quality of life)

• The Parental Stress Scale (PSS)

• Questions about family atmosphere questions

• The Parental Frustrations Questionnaire (PFQ)

• The Child Depression Inventory (CDI)

• The Strength and Difficulties Questionnaire (SDQ). We will use the parent,

teacher and self-report (ages 11-16) versions.

• The Conners Teacher Rating Scale-Revised: short form (CTRS-R:S).

Physical measures

• Weight, height, blood pressure, pulse

Biomarkers

• Blood draw (ferritin, zinc and cholesterol)

Neuropsychological tests

• Amsterdam Neuropsychological Tasks (three subtests)

• The Monetary incentive delay task for children

Mediators/predictors

• Treatment history, duration and compliance

Child factors

• Sex, age, ethnicity, school type

• Estimation IQ

• Psychiatric diagnoses

• Tanner stage + some questions of Physical Development Scale (PDS)

• Temperament (Behavioural Avoidance and Inhibition Scale [BISBAS], Inventory

of Callous and Unemotional traits [ICU], Brief Sensation Seeking Scale [BSSS])

• DNA (blood draw)

• Cortisol in hair

• Stressful events

Parental factors

• Socio-economic factors

• The Egna Minnen Beträffende Uppfostran (EMBU)

• The Adult ADHD Rating scale (AARS)

• The Parenting Sense of Competence Scale (PSOC)

• The Maudsley Marital Questionnaire (MMQ)(subschale Marital adjustment)

Study description

Background summary

Over the past decade, we have witnessed a rapid and tremendous increase in the diagnosis of attention-deficit/hyperactivity disorder (ADHD) and in the use of medication treatments for ADHD, in particular methylphenidate. This development has received much and almost exclusively negative coverage by media, politicians and government due to concerns about overdiagnosis and overtreatment with psychostimulants.
The increased and longer use of methylphenidate contrasts heavily with the lack of data on its long-term effectiveness. In fact, Dutch multidisciplinary guidelines state that there is currently only evidence for the long-term effectiveness of methylphenidate for a treatment duration between three months and two years.
We will test the hypothesis that ongoing use of methylphenidate is superior to placebo with regard to ADHD symptom severity in children and adolescents who have used methylphenidate for two years or longer. In our study we will be able to establish whether or not long-term use of methylphenidate is still effective beyond two years of treatment.

Study objective

Primary objective: To investigate the effectiveness of ongoing treatment with methylphenidate as prescribed in clinical practice beyond two years in children and adolescents.

Secondary objectives:
(1) to investigate the effects of discontinuation of methylphenidate on a number of secondary outcome measurements (e.g. clinical improvement, withdrawal effects, sleeping behaviour, quality of life, neuropsychological task performance and biomarkers (ferritin, zinc and cholesterol).
(2) to identify predictors of treatment discontinuation and long-term outcome six months later. This includes treatment duration and compliance, child factors (i.e., presence of comorbid psychiatric problems, genetic polymorphisms, stress regulation and underaroused temperament) as well as parent factors (socio-economic status, presence of psychiatric problems, parental stress and other family factors).

Study design

A double-blinded randomized placebo-controlled multicentre discontinuation trial. The centres together will recruit 120 children or adolescents.

Intervention

The participating subjects will be randomized (ratio 1:1) to either continued use of methylphenidate or to placebo during seven weeks. Withdrawal will be gradually over a period of three weeks, followed by four weeks of complete placebo. There will be three visits, baseline, after four weeks and after seven weeks. After six months there will be a follow up by telephone.

Study burden and risks

Children who will participate in the study have all been using methylphenidate for over two years and as such study participation is not associated with any particular risks. Extra burden for the participating families is limited to three visits to the clinical centre (respectively +/- 120, 60 and 120 min), an interview by telephone with the parent (+/- 45 min), two blood draws by venepuncture (30ml each), a single collection of hair strands from the child and neuropsychological tests during two visits (+/- 60 min, this time is included in the overall time estimation as mentioned above). Besides that, the parents, the child and the teacher of the child have to complete a number of questionnaires (parents: +/- 80 min at baseline, +/- 35 min at follow-ups; child +/- 45-60 min at baseline, +/- 25-15 min at follow-ups; teacher +/- 20 min at each visit). Risks will be negligible and physical discomfort mild. The research protocol includes the participation of minors as methylphenidate is primarily indicated for treatment of attention and hyperactivity problems in children.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

• Children between the ages of eight to eighteen, any ethnicity or cultural background.
• Children with their first prescription of any form of methylphenidate at least two years ago.
• Children who are for at least the last four weeks the subject has been using methylphenidate in the form of Concerta 36 mg or 54 mg.
• Children with an IQ > 70 (based on a previous IQ test or attending regular education).
• Parents (or the legal guardian) and children (>= twelve years) have provided informed consent to participate in the study.

Exclusion criteria

• Children who have not been using of methylphenidate for a continuous period > 2 months during the last two years.
• Children of parents who are planning to start new psychosocial or pharmacological therapies during the blinded period.
• Children and or parents who are unable to understand or comply with the protocol.
• Children who have any other significant disease or disorder which, in the opinion of the investigator, may either put the participants at risk because of participation in the study, or may influence the result of the study, or the participant*s ability to participate in the study.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-09-2015
Enrollment:	120
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Concerta
Generic name:	methylphenidate
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-05-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-06-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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: 27718
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2014-002002-20-NL
CCMO	NL49436.042.14
OMON	NL-OMON27718