Medication Optimization for ADHD: MOVA study. Implementation and evaluation of double-blind placebo-controlled titration in clinical practice

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Developmental disorders NEC
Study type	Interventional

Summary

ID

NL-OMON46942

Source
ToetsingOnline

Brief title
MOVA

Condition

- Developmental disorders NEC

Synonym
ADHD, attention-deficit/hyperactivity disorder

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit

Source(s) of monetary or material Support: Innovatiefonds Zorgverzekeraars

Intervention

Keyword: ADHD, methylphenidate, randomized controlled trial, titration

Outcome measures

Primary outcome

The primary outcome measures are:

-number of placebo and non-responders detected

-ADHD symptoms measured with questionnaires

-side effects measured with questionnaires

Secondary outcome

The secondary outcome measures are:

-satisfaction of parents, teachers and therapists on the titration method

-symptoms of CD and ODD, social-emotional functioning

Study description

Background summary

ADHD is one of the most common child psychiatric disorders, with a prevalence of around 5% (Polanczyk e. a, 2007). It is associated with significant negative consequences in different functional domains and quality of life (for example at home, school, work) (Shaw and others, 2012; Dabon e. a; 2010). The outcome is improved by treatment. Drug treatment is usually involves the use of stimulants, with as first choice methylphenidate. The treatment of ADHD with stimulants is effective in about 75% of the cases (Award 1992). The variability in the response, however, is large and can*t be predict well (Bang et al 1995). To obtain an optimal drug treatment, it is important to titrate with different doses, use checklists during medication evaluation, and include proactive and standardized questioning about possible side effects and using a concept with room for improvement with a constantly try to optimize the effect of the medication on the symptoms. (Verhulst and others, 2014). Making decisions about the treatment is often considered as complicated and time-consuming by

practitioners and research shows that certainly not all practitioners apply this strategy (Kovshoff and others, 2012).
In addition, there are social concerns about the number of children with ADHD in Netherlands that are being treated with methylphenidate (see Report Health Council of the Netherlands, 2014). Data show that in the last ten years the number of prescriptions for methylphenidate has quadrupled to around 4.5% of all children and young people. This percentage is almost as high as the prevalence of ADHD (about 5%), while according to the guidelines not all children with ADHD should be treated with methylphenidate. Overtreatment with methylphenidate should be reduced so children would not unnecessarily expose to negative side effects. The current guidelines recommend to use stepwise titration for the titration of methylphenidate. In this form of titration the dosage is gradually raised to the proper dosage. A higher dose will be given when a lower dose does not have the desired effect. Stepwise titration has, however, some important weaknesses.
First, it is not possible to objectively determine whether methylphenidate is sufficiently effective. This is a real problem, because a large-scale study has shown that treatment with methylphenidate at about ten percent of children with ADHD is not effective (non-responders) and that an additional 13% methylphenidate no more effect than placebo (placebo-responders) (Greenhill et al., 2001; Vitiello et al., 2001). There is substantial evidence that up to a third of the children treated with methylphenidate in the Netherlands is treated unjustified, given the above alarming figures about methylphenidate use. A second weakness is that the method does not double-blind, because parents and practitioner know that the dosage goes up, which may be an expectation effect (placebo effect). The optimal dose is not objectively defined. This is a worrisome, because many children will not get the correct dosage of methylphenidate (Greenhill et al., 2001) and an incorrect dosage reduces the effectiveness and safety of drug treatment.

Study objective

The primary goal of this study is to investigate whether placebo-controlled double-blind titration leads to optimizing the use of methylphenidate. This by detecting placebo-and non-responders more efficiently and by treating responders better so they have better controlled ADHD behaviors and fewer side effects.
The second objective of this research is to make double-blind titration easier implementable by means of the application. The satisfaction of parents, teachers and therapists will be investigated in comparison with the current stepwise titration.

Study design

This project is a RCT (Randomized Controlled Trial) with two arm design: a drug treatment optimal titrated by the practitioner with support off the application

(N = 70) and a drug treatment, through step-by-step titration, as is commonly used in the treatment centers (N = 70).

Intervention

The children in the control arm will have a gradual titration of methylphenidate, according to the protocol of the participating centers. The children in the placebo-controlled double-blind titration group will be treated according to the protocol of the study medication by their own practitioners. The optimal dose methylphenidate is determined by means of a double-blind randomized placebo-controlled titration procedure. It starts with an open lead-in phase where the child gets different doses (5 mg, 10 mg, 15/20 mg) methylphenidate in ascending order. In this phase side effects will determine whether a child can participate in the titration according to the study protocol. When the highest dose is not tolerated it will be replaced by the 2nd highest dose during the titration. If a child does not tolerate multiple doses the child can*t participate in the titration and will be further treated by the Centre. During the titration phase the child gets administered methylphenidate, 3 times a day with a fixed ose for each week with 5 mg, 10 mg, 15/20 mg (depending on the weight, children lighter than 22 kg: 15 mg) or a placebo in a random order for 4 weeks.The highest dosage will never be given immediately after the placebo. Parents and teachers register each week the effects of the medication on the behavior through the application by means of questionnaires (for inattention, hyperactivity-impulsivity, oppositional behavior and side effects). After 4 weeks the practitioner chooses the optimal dose with the application. The child is classified as ' responder ', ' placebo responder "or" non-responder '. A child is a responder if the ADHD symptoms reduce significantly during the use of at least one of the dosages methylphenidate compared to the use of placebo. Low symptom scores and no room for improvement in all dosages, indicate a placebo responder. If there is room for improvement at all doses but no significant difference between the methylphenidate dosages and placebo, the child is classified as non-responder. The children are 6 months further treated by their own practitioner and after 6 months there is new evaluation. Non-responders are further handled within the institution, but do still take part in the intervention period for the ' intention to treat analysis. We expect that 70-80% of the children is a responder and that 20-30% of children either in the placebo responder or category in the category non-responder falls

Study burden and risks

There are no known risks associated with participation to this study. There is an extra time effort to parents and teachers asked to fill out questionnaires (10-15 min per week) during the titration . More extensive questionnaires (15 min-20 min) have to be completed before the start of the titration, after the titration and after 6 months.

Contacts

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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 age of 6 and 12 with a DSM-based ADHD diagnosis, with a clinical indication to start pharmacological therapy with short-acting methylphenidate

Exclusion criteria

- counter-indication for the start-up of methylphenidate (e.g. cardiac problems)
- treated with MPH in the last 4 weeks.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-05-2017
Enrollment:	140
Type:	Actual

Medical products/devices used

Generic name:	webapplication
Registration:	No
Product type:	Medicine
Brand name:	methylphenidate
Generic name:	methylphenidate
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	22-03-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	24-04-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-08-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2016-002474-13-NL
CCMO	NL57836.029.16