Off-label use of Risperidone in Children and Adolescents (ORCA): a double-blind placebo-controlled discontinuation trial

Published: 12-10-2015
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Primary Objective: To investigate the behavioral effects of controlled discontinuation as well as the feasibility of discontinuing currently ongoing treatment with risperidone in children and adolescents with behavioral problems who have used...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Psychiatric and behavioural symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON44901

Source
ToetsingOnline

Brief title
Discontinuation of risperidone in children and adolescents

Condition

- Psychiatric and behavioural symptoms NEC

Synonym
long-term off-label risperidone treatment, No specific condition

Research involving
Human

Sponsors and support

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

Intervention

Keyword: children, discontinuation trial, randomized controlled trial, risperidone

Outcome measures

Primary outcome

The primary outcome measure will be the D-total score of the Nisonger Child

Behavior Rating Form-Typical IQ (NCBRF-TIQ).

Secondary outcome

- Strength and Difficulties Questionnaire (SDQ)

- Retrospective Modified Overt Aggression Scale (R-MOAS)

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

- Clinical Global Impression Scale (CGI)

- Children's Global Assessment Scale (CGAS)

- Kindl-R (quality of life)

- Parental Frustration Questionnaire (PFQ)

- Amsterdam Neuropsychological Tasks (ANT)

- UKU side effect rating scale (UKU-SERS)

- Abnormal Involuntary Movement Scale (AIMS)

- Barnes Akathisia Scale (BARS)

- Unified Parkinson's disease rating scale (UPDRS)

- Sleep Disturbances Scale for Children (SDSC)

- appetite and life style

- Physical Activity Questionnaire (PAQ)

- Physical measures: length, weight, waist circumference, heart rate and blood

pressure

- Blood counts

* Metabolism: fasting glucose, insulin, triglycerides, high-density

lipoproteins (HDL), low-density lipoproteins (LDL), leptine, and total

cholesterol.

* Endocrine parameters: prolactin and testosterone.

* Thyroid function: TSH and T4.

* Kidney function: creatinine, sodium, and potassium.

* Pharmacokinetics: risperidone and 9-hydroxyrisperidone concentrations.

* Albumine levels.

Predictor variables:

- Demographic data and socio-economic status

- Treatment history and psychiatric diagnosis

- Tanner stages of pubertal development

- Parent-rating scale for Reactive and Proactive Aggression (PRPA)

- Nijmeegse OUderlijke Stress Index - kort (NOSI-K)

- Alabama Parenting Questionnaire (APQ)

Study description

Background summary

Over the past decades, risperidone has been increasingly prescribed to children and adolescents on an off-label basis, while long-term effects have been insufficiently investigated and discontinuation of long term use need not lead to behavior deterioration and might have several health benefits. In our study we will investigate whether or not continued long-term use of risperidone is still effective beyond one year of treatment and what the effects of

discontinuation are on behaviour and health.

Study objective

Primary Objective:
To investigate the behavioral effects of controlled discontinuation as well as the feasibility of discontinuing currently ongoing treatment with risperidone in children and adolescents with behavioral problems who have used risperidone for at least one year.

Secondary objectives:
(1) to investigate the effects of discontinuation of risperidone on a number of secondary outcome variables (problem behavior and comorbidity, clinical improvement, general functioning and quality of life of the child, parental and family functioning, and neuropsychological functioning) and tolerability ratings (side effects and withdrawal effects, physical measures, and blood values).
(2) to identify moderators and predictors of treatment discontinuation and long-term outcome six months later. This includes treatment duration and compliance, child factors (age, sex, presence of comorbid psychiatric problems, temperamental traits, biologic factors) as well as parent factors (socio-economic status, parental and family factors).

Study design

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

Intervention

The participating subjects will be randomized (ratio 1:1) to either continued use of risperidone or to placebo during sixteen weeks. Subjects will first be switched to study medication in their regular dose for two weeks. Withdrawal will subsequently be gradually over a period of six weeks, followed by eight weeks of complete placebo. There will be four visits: pre-baseline, at baseline, eight weeks and fourteen week after. After six months there will be a follow up by phone. In subjects who have stopped their discontinuation schedule based on behavioral worsening, the measurements of the 14th week follow-up will be scheduled as soon as possible after stopping taking the study medication. If this occurs before the eight-week visit, these measurements will be cancelled.

Study burden and risks

All participating children/adolescents will use risperidone at study entry, so we do not expect any unknown risks regarding the use of risperidone. With

regard to the discontinuation of risperidone we expect some deterioration of behavioral symptoms. Subjects can stop with participating in the trial at any point of time and start their regular medication if the symptoms are too much of a burden. We accept a modest worsening of behavior, but the PI can decide further participation in the study is no longer safe based on clinical judgement.
The study includes physical examination and blood draws as well as questions and questionnaires. All study procedures are designed to minimize burden of the subjects. Invasive examinations have been reduced to a minimum to minimize burden (e.g. frequency of blood-drawing). Study staff is experienced in child and adolescent psychiatry and pediatrics. We will act towards study participants in such a way as to minimize pain, distress and fear, while at the same time have taken measures and approaches to maximize scientific benefit (e.g. collecting several blood samples for chemistry etc. by one puncture of the vein). Local anesthetics (e.g. cream) can be provided for minimizing pain by blood drawing. No examination will be conducted against the will of the subject or the caregiver. Any clinically relevant presentations will be managed in a clinically appropriate way by each study site.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
* Be between the ages of six and seventeen years and eight months
* Current risperidone use * one year.
* Current risperidone doses * 5 mg/day.
* 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

A potential subject who meets any of the following criteria will be excluded from participation in this study:
* Risperidone was discontinued for * two months in the last year.
* Current psychosis.
* Pregnancy.
* Risperidone is primarily used for the treatment of psychosis or tics.
* Having parents who are planning to start other psychosocial and pharmacological therapies during the blinded period.
* Having parents who are unable to understand or comply with the protocol.
* Presence of 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 results 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):	22-01-2016
Enrollment:	120
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	risperidone
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	12-10-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-10-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-02-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-04-2016
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-11-2017
Application type:	Amendment
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: 20175
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2014-003651-54-NL
CCMO	NL52899.042.15
OMON	NL-OMON20175