Safety and pharmacokinetics of antipsychotics in children with autism

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Personality disorders and disturbances in behaviour
Study type	Observational invasive

Summary

ID

NL-OMON47545

Source
ToetsingOnline

Brief title
SPACe

Condition

- Personality disorders and disturbances in behaviour

Synonym
autism;behavioral disturbances

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: antipsychotics, children, pharmacokinetics, safety

Outcome measures

Primary outcome

First, a pharmacokinetic (PK) model is built, linking dosage to drug plasma levels.

Second, in the pharmacodynamic (PD) analysis we will investigate the relation between the pharmacokinetic model and weight change.

Secondary outcome

In a second pharmacodynamic (PD) analysis we will investigate the relation between the pharmacokinetic model and cardiac changes, extrapyramidal symptoms, metabolic abnormalities, somnolence and clinical effectiveness.

We will also verify the relationship between DBS and venipuncture measurements of drug plasma levels in a small subgroup of children.

Study description

Background summary

Antipsychotics are the cornerstone in the treatment of behavioural problems in children with autism spectrum disorder. Unfortunately, treatment with anti-psychotics is associated with a number of serious side effects. Extrapyramidal side effects are irreversible and have a very negative impact on adherence. Metabolic abnormalities are of even greater concern because they increase the risk of diabetes and cardiovascular problems considerably. In adults there is evidence that dosing antipsychotic drugs according to Therapeutic Drug Monitoring (TDM) may reduce side effects. TDM may be even more important in children because they are experiencing rapid changes in their development. However, there are no studies that have looked at the association

between antipsychotic plasma concentrations and both efficacy and side effects in children.

Study objective

Our main objective is to develop a pharmacokinetic safety window in children and adolescents for the three most prescribed antipsychotics in the Netherlands, risperidone, pipamperon and aripiprazole. To this end we will study the relation of the measured pharmacokinetic parameters with weight change and extrapyramidal side effects over a 6 month period using a minimally invasive Dry Blood Spot technique (DBS).
As a secondary objective, we will investigate the relation between the plasma levels of the antipsychotics and cardiac changes, metabolic abnormalities, somnolence and clinical effectiveness.

Study design

We will conduct a multicentre, prospective, observational cohort study. No study intervention will occur. We will include 50 patients in each treatment group which will be followed for 6 months. In this period, extrapyramidal, metabolic and cardiac parameters are monitored. At 2 moments, we will obtain a plasma day curve of the antipsychotic agent with the Dried Blood Spot (DBS) technique.

Study burden and risks

Monitoring of metabolic status by registration of physical parameters are standard clinical practice in most treatment centres. In the Erasmus MC regular lab check ups and monitoring of treatment efficacy by means of questionnaires is standard clinical practice as well.
Compared to standard clinical care, the following examinations have been added: 1/ ECG before start and after 6 months of study for every child (instead of on indication only). 2/ Plasma day curves of the agents under study, using the minimally invasive DBS method, a finger prick procedure at 2 moments, consisting of 2 finger pricks a day. 3/ Two extra venipunctures 4/ The Epworth Sleepiness Scale which takes 2-3 minutes to complete and focuses on daytime sleepiness. 5/ Observation scales that are completed by the treating physician and only takes several minutes.
The risks are negligible and only include local irritation from the fingerprick. As a benefit, the intensified and standardised follow-up might facilitate early detection of side effects. Moreover, should the study succeed in demonstrating a relationship between drug plasma levels and side effects, side effects in this vulnerable group may be limited in the future in a minimally invasive way.
The study cannot be performed in adults, due to development-specific aspects of

both the pharmacokinetic and pharmacodynamics processes.

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)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

- Age 6 to 18 years
- Documented clinical diagnosis of autism spectrum disorder according to DSM IV or DSM V and comorbid behavioural problems
-Treated with either aripiprazole, risperidone or pipamperone

Exclusion criteria

- Diabetes type I or II
- Congenital or acquired syndrome associated with changes in appetite, body weight or lipid profile (e.g. Prader Willi)
- Treatment with another antipsychotic within the last 6 months
- Known Long QT syndrome (LQTS)

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-08-2016
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	12-05-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	27-10-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	09-12-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-12-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-03-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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: 22814
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL56247.078.16
OMON	NL-OMON22814