Saliva pharmacokinetics of methylphenidate (MPH) following ingestion of immediate and sustained release formulations in children with attention- deficit hyperactivity disorder (ADHD)

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Objective: Main objective of this study is to compare the area under the MPH saliva concentration versus time curve (AUC) following ingestion of immediate and sustained release formulations of MPH in children with ADHD. Secondary objectives are: 1....

Ethical review	Not approved
Status	Will not start
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Observational invasive

Summary

ID

NL-OMON37735

Source
ToetsingOnline

Brief title
SALMIAC (SALiva Methylphenidate In Adhd Children)

Condition

- Hypothalamus and pituitary gland disorders
- Personality disorders and disturbances in behaviour

Synonym
ADHD, attention deficit hyperactivity disorder

Research involving
Human

Sponsors and support

Primary sponsor: Maasstadziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W,bijdrage fonds kindergeneeskunde Maasstadziekenhuis

Intervention

Keyword: ADHD, hormones, methylphenidate, Saliva

Outcome measures

Primary outcome

The main study endpoint is the area under the MPH saliva concentration versus

time curve (AUC) following ingestion of a formulation with immediate and

sustained release MPH.

Secondary outcome

a. The time profiles of the hormones cortisol, testosterone and DHEA in saliva

following the two different formulations.

b. The genetic difference in esterase activity between individuals

c. The relationship between saliva MPH concentration and clinical effect and

hormone concentration

d. The correlation between MPH concentrations in saliva and plasma

Study description

Background summary

Rationale: Attention- deficit hyperactivity disorder (ADHD) is one of the most frequently encountered psychiatric disorders in the pediatric out clinic. In the Netherlands the incidence of ADHD is 5% and half of the patients have

received or receive pharmacotherapy1,2. The drug of first choice is methylphenidate (MPH). Little is known about the pharmacokinetics and pharmacodynamics of MPH in children due to medical-ethical issues when performing pediatric clinical trials. MPH is metabolized by esterases that can be measured in DNA from saliva. Slow, normal ad extensive metabolisers exist which can discriminated on basis of their genotype.
MPH therapy is routineously initiated with an immediate release formulation. Subsequently, children are switched to a dose-equivalent formulation with sustained release. MPH sustained release formulations are preferred above immediate release preparations since they have to be taken less frequently, which favors drug adherence. In clinical practice however, the switch of formulations results in less efficacy in some patients while other patient experience more adverse effects. This difference may be due to differences in bioavailability of the formulations or to fluctuating plasma levels during the day.
In a recent study differences have been observed in the time profiles of hormonal concentrations in saliva (cortisol, testosterone, dehydroepiandrosteron (DHEA)) in children with ADHD when compared to healthy controls3,4,5. These differences may be important with respect to behavior and the development of children with ADHD, which is delayed compared to healthy controls.

Study objective

Objective: Main objective of this study is to compare the area under the MPH saliva concentration versus time curve (AUC) following ingestion of immediate and sustained release formulations of MPH in children with ADHD. Secondary objectives are: 1. The comparison of time profiles of the hormones cortisol, testosterone and DHEA for the different formulations The profiles will be compared to the profiles of the children before starting medication. 2: Evaluation of the relationship between the esterase genotype and MPH clearance and elimination halflife.

Study design

The study is designed as an observational study. Children diagnosed with ADHD (6 to 18 year) who are visiting the paediatric outpatient clinic of the Maasstadziekenhuis will be asked to participate. Participating patients will receive MPH therapy according to clinical routine. Therapy is started with an immediate release formulation of MPH and the MPH dose is individually titrated. After optimal titration with no undesirable side effects the patient is routinely advised to switch to a sustained release formulation.

Separate saliva concentration versus time profile of MPH and the hormones will be assessed for both the immediate release and sustained formulation. Each patient will serve as its own control.

The saliva pharmacokinetics of MPH will be investigated for 4 sustained release formulations (Concerta®, Equasym XL® , Medikinet CR® of methylfenidaat Retard-Regenboogapotheek), which are all registered for the treatment of ADHD. In each child the pharmacokinetics of only one sustained release form will be studied. For each formulation 10 children will be included, so a total of 40 children will be included for the whole study.

The time profiles of the hormones cortisol, testosterone and DHEA in saliva will be assessed before the start of MPH therapy and for both the immediate release and sustained formulation. A partictipating patient will provide 3 saliva curves: pretreatment, immediate release and sustained release.

Study burden and risks

no risks are involved, the study burden is low

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

ADHD
6-18 y

Exclusion criteria

no ADHD
<6 y

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Ethics review

Not approved

Date:	27-02-2013
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (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

No registrations found.

In other registers

Register	ID
CCMO	NL38518.101.11