The difference in pharmacodynamic and pharmacokinetic profiles between Tentin and magistral dexamphetamine in adults with attention deficit hyperactivity disorder, a double blinded randomised crossover-controlled trial.

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

Summary

ID

NL-OMON53816

Source
ToetsingOnline

Brief title
DAVE

Condition

- Cognitive and attention disorders and disturbances

Synonym
ADHD, attention deficit hyperactivity disorder

Research involving

Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: attention deficit hyperactivity disorder, dexamphetamine, pharmacodynamics, pharmacokinetics

Outcome measures

Primary outcome

- Quantified behaviour Test for analysis of objective effects.

- Blood samples for analysis of the plasma concentration of dexamphetamine.

- Autonomic and adverse effects measurements (vital signs): Blood pressure and

Heart rate

Secondary outcome

Subjective effects:

- Addiction Research Centre Inventory (ARCI) - Acute Subjective Response to

Substances (ASRS): Amphetamine Scale (9-11)

- Bond-Lader Visual Analog Scale (BL-VAS)

- QbTest performance questionnaire

Study description

Background summary

For a long time, dexamphetamine 2.5 mg (magistral) was only available as an unregistered drug prepared by local pharmacies in the Netherlands. This situation changed in 2016 when the brand-name Amfexa 5 mg was brought to the market. In 2020, the manufacturer changed the name Amfexa to Tentin, while the

composition remained the same. The brand-name drug Tentin (Amfexa) should have the same effect as the unregistered drug prepared by a pharmacy, since the active compound, dexamphetamine, is identical in both tablets.

The Dutch Pharmacovigilance Centre Lareb identifies side effects associated with the use of medicines in daily practice and it is the Knowledge Centre for adverse drugs reactions (ADRs). Following the conversion of magistral dexamphetamine (GD) to Tentin (Amfexa), Lareb has received a substantial number of reports for Tentin (dexamphetamine). The same increase in adverse reaction reports is also reported at EudraVigilance. The reported side effects associated with Tentin (Amfexa) use have been assessed by the Medicines Evaluation Board (College ter Beoordeling van Geneesmiddelen) and Lareb, which has not led to warnings regarding the safety of the drug or the quality (tablet contents; excipients) of Tentin. The Medicines Evaluation Board (CBG) and Lareb regard the number of reports as a consequence of nocebo effects, and thus psychological rather than pharmacological effects, where patients expect a negative effect, in this case side effects, by switching to another brand(name), despite the fact that the active compound and dosing has remained the same.

Another possible cause for the reported complaints can be sought in a difference in absorption and dissolution rate between Tentin and magistral dexamfetamine. Patients reported side effects that can be explained by delayed absorption of Tentin, such as ineffective/decreased/incomplete therapeutic effects, insomnia, restlessness, disturbance in attention and experiencing negative emotions. A delayed absorption can be caused by a lower dissolution rate, which might be caused by the excipients or the preparation method of the product. Other frequently reported complaints such as a headache, migraine, palpitations, and the rebound effect can be explained based on the moment and height of the peak concentration.

No previous studies were found comparing the pharmacodynamic (Pd) and pharmacokinetic (Pk) profile of Tentin with magistral dexamphetamine.

Study objective

The primary objective is to compare the pharmacological profile of the magistral form of dexamphetamine sulphate to the pharmacological profile of the brand-name form of dexamphetamine (Tentin©) in adult patients diagnosed with attention deficit hyperactivity disorder (ADHD) and assess whether there is a difference between the pharmacodynamic (Pd) and pharmacokinetic (Pk) profile of Tentin and magistral dexamphetamine.

The secondary objective is to assess how pharmacokinetic variability influences the objective and subjective (side) effects experienced by adult patients with ADHD.

Study design

Double blinded randomised crossover-controlled trial

Intervention

The study includes a (digital) screening and two intervention days. Participants will receive one intervention on each intervention-day. All participants will receive GD and Tentin©, dosed as prescribed by the practitioner, in a randomised order for two intervention-days. At three moments (0, 60 and 120 minutes after drug administration) on each intervention-day, participants will complete the QbTest to assess objective performance and the QbPerformance to assess subjective performance. At eight moments (0, 45, 60, 75, 90, 120, 150 and 180 minutes after drug administration) on each intervention-day, participants will fill out questionnaires to assess subjective experiences. At eight moments (0, 45, 60, 75, 90, 120, 150 and 180 minutes after drug administration) on each intervention-day, participants will undergo blood sampling to determine dexamphetamine plasma-concentrations and vital sign measurements for safety monitoring and possible outcome-effects.

Study burden and risks

The burden of participating in this study include:
I. General time spent on participation
- One (digital) meeting: participant informing, informed consent and screening.
- Two visits to the outpatient clinic: two intervention days.
II. Activities and sampling
- Filling out questionnaires
- Take six QbTests in total over two days (3 tests on each day).
- Taking a total of sixteen blood samples (2ml per sample) over a period of two days (eight samples on each intervention-day).

The therapy given during this study is based on the treatment as usual (TAU). Participants will receive Tentin© and magistral dexamphetamine as prescribed by their practitioner. The burden for each participant is considered minor and the risk of adverse events very low. Participants will undergo a total of sixteen blood samples (2ml per sample), eight per intervention day. The risk of complications and adverse events regarding blood sampling is acceptable in relation to the possible benefits that may be gained from this study, i.e., improved pharmacotherapy guidelines for adult patients with ADHD. A benefit for the participant lies in the fact that his or her personal response to stimulants is documented and as such can be used for future pharmacotherapeutic decisions.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

To be eligible to participate in this study, a subject must meet all the following criteria:
- Participant is aged 18-64 years at time of screening.
- Participant is diagnosed with ADHD according to the DSM 5 criteria.
- Participant has switched from Tentin© to magistral dexamfetamine due to the adverse effects of Tentin.
- Participant is being treated adequately with dexamphetamine, as determined by their practitioner, at time of screening.
- Participant is able and willing to provide written informed consent.
- Participant is able and willing to comply with the study protocol (e.g. swallow capsules, have blood samples taken, can visit the outpatient clinic twice).

- Participant has not participated in another study in the past three months.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Participant has a disorder that might affect drug absorption (e.g. gastrointestinal, metabolic, endocrine or liver disorder).
- Participant is allergic to the ingredients of the capsules.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-06-2023
Enrollment:	26
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dexamfetamine sulphate
Generic name:	Dexamfetamine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tentin

Generic name:	Dexamfetamine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	02-03-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-04-2023
Application type:	First submission
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	EUCTR2022-003237-19-NL
ClinicalTrials.gov	NCT05621174
CCMO	NL82695.018.22