TOwaRds PrEcision Dosing of Olanzapine in anorexia nervosa patients

Published: 22-02-2023
Last updated: 04-04-2025

Objective: In this study we propose elucidating the pharmacokinetics of olanzapine in AN patients, to optimize the dosing strategy, to the extent of increasing the efficacy and reducing the risk of side effects. To this end, we will assess the…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Eating disorders and disturbances
Study type	Observational invasive

Summary

ID

NL-OMON53540

Source
ToetsingOnline

Brief title
TORPEDO

Condition

- Eating disorders and disturbances

Synonym
Anorexia nervosa

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Funding by the hospital pharmacy

Intervention

Keyword: Adolescent, Antipsychotic, Pharmacokinetic, Therapeutic drug monitoring

Outcome measures

Primary outcome

Main study parameters/endpoints: We aim to assess the pharmacokinetic parameters of olanzapine in AN patients. To this end, we will assess the pharmacokinetic differences of olanzapine between AN and non-AN patients, in adolescents and young adults.

Secondary outcome

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

Study description

Background summary

Rationale: Anorexia nervosa (AN) is a debilitating eating disorder with one of the highest mortality rates of all psychiatric disorders. In the Netherlands, over 5.600 patients suffer from AN. The incidence rate is 1300 per year and this number is still increasing. The path toward full recovery is often long and only half of the patients recover completely after 10 years. As part of the treatment of AN, olanzapine is frequently used to reduce severe anxiety, agitation, and obsessive compulsions. Due to a dearth of pharmacokinetic studies on olanzapine in this population with altered body composition, and the limitations of side effects, doctors often doses low out of precaution. This may result in subtherapeutic treatment and elongates the progression and the treatment.

Study objective

Objective: In this study we propose elucidating the pharmacokinetics of olanzapine in AN patients, to optimize the dosing strategy, to the extent of

increasing the efficacy and reducing the risk of side effects. To this end, we will assess the pharmacokinetic differences of olanzapine between AN, and non-AN patients, in adolescents and young adults.
We will investigate the relationship between the plasma levels of olanzapine in steady state and side effects such as extrapyramidal symptoms (SAS), cardiac abnormalities (ECG), sedation, and metabolic changes (full lipids spectrum).

Study design

Study design: We will conduct a multicenter cross-sectional study.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit, and group relatedness:
This study is a non-interventional, observational study. The extra burden for the participant includes 3 finger pricks and extra questionnaires (depending on the questionnaires that are standard care in the participating center). Besides local irritations of the finger pricks, the overall risks of these measurements are negligible. The intensified and standardized follow-up might facilitate early detection of side effects in participating patients. 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 by personalized therapeutic drug monitoring. Given the promising position of olanzapine in the treatment of this persisting and debilitating disease, this might be of high societal benefit.

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)

Inclusion criteria

AN group
• Age 12 to 30 years
• Diagnosis according to DSM-5 criteria for anorexia nervosa
• Documented clinical indication for treatment with olanzapine
• Treatment with olanzapine (including current users and recent starters)
• Signed informed consent

Non-AN group
• Age 12 to 30 years
• Documented clinical indication for treatment with olanzapine
• Treatment with olanzapine (including current users and recent starters)
• Signed informed consent

Exclusion criteria

AN group
• Co-medications: carbamazepine, lopinavir, rifampicin, ritonavir, ciprofloxacin and fluvoxamine.
• Pregnancy
• The congenital or acquired syndrome is associated with changes in appetite, body weight, or lipid profile (e.g. Prader Willi)

Non-AN group:
• Diagnosis according to DSM-5 criteria for anorexia nervosa
• Co-medications: carbamazepine, lopinavir, rifampicin, ritonavir, ciprofloxacin and fluvoxamine.

• Pregnancy
• The congenital or acquired syndrome is associated with changes in appetite, body weight, or lipid profile (e.g. Prader Willi)

Study design

Design

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:	Recruiting
Start date (anticipated):	08-11-2023
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	22-02-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	22-11-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	16-07-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-01-2025
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

No registrations found.

In other registers

Register	ID
CCMO	NL82751.078.23