Pharmacokinetics of Lorazepam Oral Liquid in Paediatric ICU Patients

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON44702

Source
ToetsingOnline

Brief title
LORA01

Condition

- Other condition

Synonym
physical dependence, withdrawal

Health condition

lichamelijke afhankelijkheid van een sedativum

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Intensive care, Lorazepam oral liquid, Pedriatic, pharmacokinetic

Outcome measures

Primary outcome

The primary aim of this study is to characterize the pharmacokinetic parameters

CL, Vd, Cmax, tmax, F and ka of lorazepam using the newly developed lorazepam

oral solution 1 mg/ml in infants and children

Secondary outcome

The secondary study parameters are:

- to explore the impact of clinical and genetic co-variates on pharmacokinetic

parameters,

- to evaluate the withdrawal protocol by monitoring occurrence of symptoms of

withdrawal with use of the Sophia Observation withdrawal Symptoms (SOS) scale,

- to assess acceptability and safety of the lorazepam liquid formulation.

Study description

Background summary

After prolonged use of sedative drugs at the paediatric intensive care unit, children are switched to oral lorazepam in clinical practice, to prevent withdrawal symptoms and facilitate tapering of the sedatives. The current weaning guideline, including the conversion to equipotent lorazepam dosages, has been derived from PK/PD data from adult patients and the impact of ontogeny on the conversion has not yet been assessed. No standardised oral liquid formulation of lorazepam has been available for use during weaning.

In this study we aim to generate pharmacokinetic data of lorazepam in children to optimise the dose-conversion in the weaning guideline in different age-groups, using a newly-developed standardised oral liquid formulation of lorazepam.

Study objective

The primary objective of this study will be to determine the pharmacokinetic profile of lorazepam oral liquid 1 mg/ml in the paediatric ICU population, with specific attention for the population aged up to 12 years of age.

The secondary objectives are:
* to explore the impact of clinical co-variates on pharmacokinetic parameters,
* to assess the occurrence of symptoms of withdrawal with use of SOS scale,
* to assess the occurrence of over- and undersedation with use of the COMFORT-B scale and Nurses* Interpretation of Sedation Score.
* to use the observed pharmacokinetic data to optimize the current withdrawal protocol,
* to assess the acceptability and safety of the lorazepam liquid formulation,
* to explore the impact of UGT2B15*2 SNP on pharmacokinetic variability.

Study design

Single center, cross-over, non-randomised, pharmacokinetic study

Intervention

All patients are switched to lorazepam according to current clinical practice. The first dosage of lorazepam is administered intravenously, and the following dosages are administered orally using the standardized lorazepam oral liquid. Children currently treated with oral lorazepam are switch to study medication.

Study burden and risks

Lorazepam is given with therapeutic intent and all patient will be treated with lorazepam in regular dosages, irrespectively of their participation in the study. However, only in the study they will receive lorazepam as an oral liquid. This new lorazepam oral solution is well validated and tailored to the specific needs of the paediatric population including acceptable palatability, dose flexibility, ease of administration and use of appropriate pharmaceutical excipients.

The first dosage of lorazepam is administered intravenously in the study, in order to obtain a full pharmacokinetic profile. The burden of this administration will be minimal as an intravenous access will still be in place

and the lorazepam is administered with therapeutic intent. The subsequent oral dosages will be administered as a standardised oral liquid, which replaces individual extemporaneously prepared capsules or orally administered iv fluid, both of which are not validated for this use. During both iv and oral use, 3 blood samples are drawn to determine blood levels of lorazepam. Blood sampling will be combined with blood sampling for clinical care as much as possible. The occurrence of withdrawal symptoms is monitored and treated as routine clinical care.
All procedures are outweighed against the benefits of the study and the availability of oral lorazepam liquid for the paediatric population.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

* aged below 12 years old,

* signed consent from the parent or legal assent,
* admitted to the Sophia Children's Hospital,
* scheduled to start the weaning protocol with oral lorazepam, or
* currently treated with lorazepam.

Exclusion criteria

* concomitant treatment with another investigational drug,
* contraindications for lorazepam use;
-Severe liver insufficiency, defined as 5 times upper level of ALAT and ASAT
-Hypersensitivity to lorazepam,
-Myasthenia gravis

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-12-2015
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	Lorazepam (oral liquid formulation)
Product type:	Medicine
Brand name:	Temesta
Generic name:	Lorazepam

Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	19-05-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-06-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-11-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-02-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-11-2017
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
EudraCT	EUCTR2015-001043-37-NL
CCMO	NL53014.078.15