Pharmacokinetic-pharmacodynamic modeling of S(+)-ketamine in healthy volunteers

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Aims of the study:1) To obtain pharmacokinetic parameters of S(+)-ketamine;2) To study the pharmacodynamic effects of intravenous S(+)-ketamine on experimental pain;

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

Summary

ID

NL-OMON29713

Source
ToetsingOnline

Brief title
KET STUDY

Condition

- Other condition

Synonym
pain

Health condition

pijnstilling

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: TREND

Intervention

Keyword: analgesia, modeling, pain, S(+)-ketamine

Outcome measures

Primary outcome

1. Cp S(+)-ketamine

2. pain relief as tested by electrical and heat pain models.

Secondary outcome

3. EEG

5. ECG

6. Blood pressure

Study description

Background summary

The NMDA-receptor antagonist ketamine, at relatively low-dose, is a potent analgesic. It is used in the perioperative setting as well as in chronic pain, for example in the treatment of neuropathic pain and pain from malignancies. We are currently assessing ketamine*s analgesic efficacy in CRPS type 1 patients in an experimental study (protocol P05.100).

Despite its wide use, relatively little is knows about ketamine*s pharmacokinetics -PK- and pharmacodynamics -PD- or the link between the two. For example, there is no knowledge on the link parameter ke0, which is an estimate of the drugs onset and offset-times. Knowledge of ketamine*s PK and PD is needed to be able to fully understand clinical ketamine data in patients, such as CRPS type 1 patients. Furthermore, it will enable the optimization of infusion schemes and hence the treatment of patients on ketamine.

Ketamine is a racemic mixture. Recently the S(+) form became available

(Ketanest). In contrast to the racemic mixture, S(+)-ketamine shows less psychomimetic side effects. This is the reason that the S(+) form is now widely used with the racemic mixture rapidly loosing market.

In this study we will assess the pharmocokinetics and pharmacodynamics of intravenous S(+)-ketamine in healthy volunteers. This will result in a pharmacokinetic/pharmaco-dynamic (PK/PD) model which may be used to predict S(+)-ketamine concentration and pain relief after intravenous infusion.

Study objective

Aims of the study:

1) To obtain pharmacokinetic parameters of S(+)-ketamine;

2) To study the pharmacodynamic effects of intravenous S(+)-ketamine on experimental pain;

Study design

The design of the study is placebo-controlled, single-blind, randomized cross-over

Study burden and risks

Nausea

There is a chance that the subjects become nauseated. In that case they will receive 4 mg iv ondansentron (Zofran), a potent antiemetic. This will not end the study.

Psychomimetic side effects

S(+)-ketamine may cause psychedelic side effects such as hallucinations, vivid dreams, feeling of inebriation, confusion, drowsiness, and dizziness. All of these side effects are temporarily and will disappear spontaneously or after discontinuation of the S(+)-ketamine infusion. These side effects will be monitored by using the Bowdle scales.

We are currently performing a S(+)-ketamine study (P05.107) and have now some additional knowledge on the psychomimetic effects of the S(+)-variant of ketamine. The psychomimetic effects of S(+)-ketamine are minimal with some dizziness as most pronounced side effect. If side effects occur they do so only after prolonged infusion. Hence we do not expect serious problems from S(+)-ketamine with respect to psychomimetic side effects in our current study. We cannot exclude, however, that some hallucinations or vivid dreams during the

ketamine infusion occur. They will dissappear upon the termination of the infusion. In case such side effect do occur in our study, the infusion of ketamine will immediately be terminated and the study will continue without further drug infusion.

Arterial line

Due to the venous and arterial lines some bruising may occur. In rare cases, especially after prolonged placement (>> 36 hours) thrombosis or infection have been described. In this study, duration of arterial line placement is not more than 8 hours.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

healthy volunteers

Exclusion criteria

Obesity (BMI > 30);
Presence of medical disease (heart-, lung-, liver-, kidney-, neurologic disease; diabetes m.; pyrosis; diaphragmatic hernia);
Presence of psychiatric disease;
History of chronic alcohol or drug use;
Allergy to study medications;
Possibility of pregnancy; and
Lactation.

Study design

Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-09-2007
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ketanest

Generic name:	S(+)-ketamine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-07-2006
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2006-002979-40-NL
CCMO	NL13047.058.06